ERRATUM

Metabonomics and Gut Microbiota in Nutrition and Disease

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Chapter 4

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Where reference 29 is cited please note the following credit text reprinted with permission of Future Medicine Ltd from Sun J, Beger RD, Schnackenberg LK. Metabolomics as a tool for personalizing medicine: 2012 update. Personalized Medicine. 2013;10(2):149–61**.** With permission from Future Medicine Ltd.

Please also note that the following citations were omitted:

"Many phenotypic and genotypic states, such as a toxic response to a drug, are predicted by differences in the concentrations of functionally relevant metabolites in biological fluids and tissues" [14].
The previous reference was: [none].

The online version of the original book can be found at
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“Therefore, it is critical to be able to assess an individual’s metabolic phenotype, which will provide useful information for determining the correct drug and dose treatment and predicting the individual response following a therapeutic intervention.”
“The metabolic phenotype (metabotype) is a result of the overall influences of the patient’s physiological status, gut microbiome status, and chemical, genetic, and other environmental factors. Changes in the metabotype reflected in the biofluid or tissue evaluated occur downstream of alterations in gene and protein expression. As such, the metabotype, which comprises the genotype and phenotype, represents the ultimate biological endpoint and can provide useful information about an individual’s current physiological status that can be used for predicting the outcome prior to a therapeutic intervention” [29].
The previous reference was: [none].

“metabonomics provides the capability to analyze large arrays of metabolites for extracting biochemical information that reflects true functional endpoints of overt biological events, whereas other functional genomics technologies such as transcriptomics and proteomics merely indicate the potential cause for phenotypic response”. “Metabonomics bridges this information gap by depicting, in particular, such functional information because metabolite differences in biological fluids and tissues provide the closest link to the various phenotypic responses. Such changes in the biochemical phenotype are of direct interest to pharmaceutical, biotech, and health industries once appropriate technology allows the cost-efficient mining and integration of this information” [14].
The previous reference was: [none].

“necessarily predict drug effects, toxicological response, or disease states at the phenotype level unless functional validation is added” [14].
The previous reference was: [none].

“Understanding these connections, in turn, may eventually lead to more targeted nutrition or therapies and more refined disease risk stratification. These could result in a critical step towards personalized health care and nutrition based on a combination of genotyping and metabolic characterization” [14].
The previous reference was: [none].

“will provide a more personalized approach to patient treatment with a more positive outcome by diagnosing not only the disease but also the disease phenotype” [29].
The previous reference was: [none].

“The metabolic profile represents the phenotype of the organism and reflects the overall biological influences, including interactions between multiple genomes (e.g., genomes from animals or humans and their gut microbiome)”. “Pharmacometabonomics uses the pre-dose metabolite profiling in the biofluids or fecal extracts to predict the responses of an individual to a drug/nutritional intervention and to identify surrogate markers for subsequent drug administration.

Furthermore, pharmacometabonomics is capable of providing useful drug pharmacokinetic and drug metabolite information for an individual, which can provide a mechanistic understanding of varied responses between individuals to the efficacy, side effects, and toxicity of a drug" [29].
The previous reference was: [none].

"In view of the chemical and physical diversity of small biological molecules, the challenge remains in developing protocols to gather the whole "metabolome"" [14].
The previous reference was: [none].

"Metabonomics studies demonstrate its potential impact on the drug discovery process by enabling the incorporation of safety endpoints much earlier in the drug discovery process, reducing the likelihood (and cost) of later stage attrition" [14].
The previous reference was: [none].

"The metabolic profile of the pre-dose urine samples can predict both individual susceptibility to acetaminophen-induced toxicity and liver injury and also can predict the relative excretion levels of acetaminophen metabolites in the forms of glucuronide and sulfate conjugates" [29].
The previous reference was: [none].

"NMR-based metabonomics approaches were employed to profile pre- and postdose urinary metabolites and discovered that human subjects with high pre-dose levels of *p*-cresol (one of the metabolites related to an individual's gut microbiome) had lower concentrations of acetaminophen metabolites" [29]. From postdose urine samples, it was possible to determine the proportions of the various drug metabolites excreted by each subject, which was known to show considerable intersubject variation. The findings indicate that each individual, colonized by a unique assortment of trillions of microbes, responds to a drug differently, either beneficially or adversely. It provides the information of how a particular drug is metabolized and excreted by each individual. Such information may have a major influence on the drug safety and efficacy. "This study demonstrates that evaluation of a metabolic phenotype by metabolic profiling could play an important role in drug metabolism and toxicity, as well as in personalized health care" [29].
The previous reference was: [none].

"In both preclinical screening and mechanistic exploration, metabolic profiling can offer rapid, noninvasive toxicological information that is robust and reproducible, with little or no added technical resources to existing studies in drug metabolism and toxicity" [14].
The previous reference was: [none].

"The metabolome, or the complete metabolite composition of a system such as a cell or organism, is the end product not only of the genetic blueprint of an organism but also all influential factors to which the organism is exposed, such as nutrition, environmental factors, or treatments" [55].
The previous reference was: [none].

"Metabonomic strategies together with advanced chemometric and bioinformatic tools [44, 51, 52] can help track the interaction between nutrients and human metabolism, as well as the involvement of the genome and the gut microbiome, in overall human health, and can be considered critical measures of function or phenotype" [53] [55].
The previous reference was: [53].

"component of nutritional phenotypes and will enable individualized dietary recommendations. The relation between diet and metabonomic profiles as well as between those profiles and health and disease needs to be established" [14].
The previous reference was: [none].

"Many progresses are made through a systematic inventory of all relevant parameters by using different "-omics" technologies and application of new bioinformatics tools together with extensive data warehousing to unravel disease mechanisms, define biomarkers, or apply personalized medication" (Fig. 4.4) [55].
The previous reference was: [none].

"Likely, in cases of impairment of human homeostasis, the patients would thus develop a coordinated approach to reestablish a metabolic trajectory for the individual consistent with their metabolic phenotype" [55].
The previous reference was: [none].

"The results of this study highlight the diversity of physiological variations of human metabolism and emphasize the effect of nutritional phytochemicals in modulating human metabolism and maintaining homeostasis of human gut eco-system" [55].
The previous reference was: [none].

"Xie et al. [59] performed a study on 20 volunteers to investigate the human metabolic response to drinking Pu-erh tea over a 6-week period, using a UPLCQTOFMS-based metabonomics approach. The final metabolic profile was greatly altered by Pu-erh tea consumption. The trajectory of the PCA scores plot based on urine data revealed a clear separation tendency of samples obtained before (days 1 and 7), during (days 16, 21, and 28), and after tea ingestion (washout period; days 30, 36, 42). Interestingly, the metabolic patterns of samples obtained 2 weeks after tea intake are still distinct from the pre-dose pattern, probably due to the possibility that Pu-erh tea may change the structure of the resident gut microbiota" [55].
The previous reference was: [none].

This was followed by a more in-depth study of Pu-erh tea in human subjects [60]. "Urine samples were collected at 0, 1, 3, 6, 9, 12, and 24 h within the first 24 h of tea intake and once a day during a 2-week daily Pu-erh tea ingestion phase and a 2-week "washout" phase. The dynamic concentration profile of bioavailable plant molecules (due to in vivo absorption and the hepatic and gut bacterial metabolism) and the human metabolic response profile were identified and correlated with each

other, highlighting the great potential of metabonomic strategy to unravel the complex interactions between multicomponent nutraceuticals and human metabolic system in nutritional studies" [55].
The previous reference was: [none].

"The goal of nutrition has extended beyond just ameliorating or curing diseases and now aims to achieve an overall objective in preventing diseases and improving health. Therefore, the pivotal scientific objective has become understanding the relationship between diet (both macroand micronutrients) and health/diseases. The comprehensive analysis of the metabolome via metabonomics will serve as the bioinformational base for modern nutritional science. Biomarkers and/or patterns of expression will undoubtedly have the potential to be used for human health assessment (Fig. 4.5). Together this indicates that the future goal of nutritional research will be to predict the likelihood of future diseases within the context of an individual's overall heath and identify causal risk factors, leading to recommendations for appropriate intervention, such as to change dietary habits or to avoid homeostasis loss and maintain healthy status" [55].
The previous reference was: [none].

"Whereas the human genome is the set of all genes in a human being, the human metabolome is the set of all metabolites in a human being. Metabonomics bridges the gap between the genotype and the phenotype and is an important basis of personalized medicine. Metabonomics has been used to identify biomarkers for disease and the effects of drugs" [14]. Various metabonomic technologies including NMR and MS have been intensively applied to metabonomics study. "Pharmacometabonomic approach to personalizing drug treatment uses a combination of pre-dose metabolite profiling and chemometrics to model and predict the responses of individual subjects. Metabonomics also has a role to play in assessing drug toxicity and in guiding nutrition" [14].
The previous reference was: [none].

"An approach referred to as integrative personal "-omics" profile evaluated genomic, transcriptomic, proteomic, metabonomic, and antibody profiles from a single individual over a 14-month period. The study revealed changes in the "-omics" profiles between healthy and viral states and between nondiabetic and diabetic states throughout the study period. Furthermore, it was noted that disease risk could be assessed from the individual and maternal genome sequences. This study demonstrated that the integration of genomics data with other dynamic "-omics" datasets can be used to predict various medical risks and the health status of an individual. Such datasets for many individuals may provide a database that can be used for enhancing diagnostics, monitoring, and treatment in the future with metabonomics playing a critical role" [29].
The previous reference was: [none].

Chapter 9

The aim of this erratum is to acknowledge the original sources used in this book. The authors omitted a reference from the list and apologize for this oversight.

The following reference is missing from the list:
95. S Collino, FP Martin, LG Karagounis, et al. Musculoskeletal system in the old age and the demand for healthy ageing biomarkers. Mech.Ageing Dev. 2013; 134: 541-7.

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The corrected citations:
"Aging can commonly be characterized as a progressive, generalized impairment of biological functions resulting in an increased vulnerability to environmental challenge and a higher risk of disease and death" [1, 95].
The previous reference was: [1].

"Understanding the physiology of aging is of tremendous importance to allow populations to grow old disease-free and with a good quality of life. In this respect, it is important to understand the natural aging process and to elucidate where lifestyle and/or dietary interventions can have an impact" [95].
The previous reference was: [none].

"Imaging techniques and flux analysis using stable isotopes are parallel technologies to obtain metabolite information. Multivariate statistical and bioinformatics techniques are ultimately used for data mining the complex metabolic profiles which encapsulate information on genetics, environmental factors, gut microbiota activity, and lifestyle and food habits. This combined strategy sustains the complex process of identifying emerging biomarkers indicative of the individual response to specific physiological factors and/or nutritional/physical interventions" [95].
The previous reference was: [none].

"In addition, elderly may be also prone to be resistant to anabolic stimuli which is likely a key factor in the loss of skeletal muscle mass with aging [95]".
The previous reference was: [none].

"As centenarians well represent the model of successful and healthy aging [14], there are many important implications in revealing the underlying molecular mechanisms behind such acquired longevity" [95].
The previous reference was: [none].

"Untargeted metabonomics profiling of urine revealed that the longevity process is marked by changes in gut microbial metabolites, as displayed by increase urinary excretions of phenylacetylglutamine, p-cresol sulfate, and 2-hydroxybenzoate. Moreover, centenarian offsprings, who are reported to have delay in age-related diseases, have a distinct serum metabolic phenotype from siblings of non-long-living parents, with changes in amino acids (serine, phenylalanine) and lysophosphatidylcholines" [95].

The previous reference was: [none].

“Additionally, an investigation on specific lipids associated with familial longevity in females was explored by Gonzalez-Covarrubias et al. in the plasma lipidome by measuring 128 lipid species in 1,526 offspring of nonagenarians (59 years±6.6) and 675 (59 years±7.4) controls from the Leiden Longevity Study” [16,95].
The previous reference was: [16].

“Here in women 19 lipid species associated with familial longevity with ether phosphocholine and sphingomyelin species are identified as candidate longevity markers. While this population reflects a different cohort with plausible differences in lifestyle and dietary habits, common to the previous study, the authors postulated that lipid signatures in plasma lipidome of female individuals could suggest a better antioxidant capacity and lower lipid peroxidation capabilities with probable effects on the longevity process” [95]
The previous reference was: [none].

“The development of systems biology approaches and the new generation of biomarker patterns will provide the opportunity to associate complex metabolic regulations with key aging biological processes” [95].
The previous reference was: [none].

“The gastrointestinal tract (GIT) is one of the most essential interfaces of mammalian organism interacting with nutrients, exogenous compounds, and gut microbiota, and its condition is influenced by the complex interplay between these environmental factors and host genetic elements. Along the GIT, the gut microbiota is a key determinant of the gut functional ecology and metabolic homeostasis, through fine interactions with regulatory processes involved in the absorption, digestion, metabolism, and excretion of dietary nutrients as well as barrier integrity, motility, and mucosal immunity” [23, 24, 95].
The previous reference was: [23,24].

“Increasing scientific evidence has been reported on the fundamental role of gut microbiota in both positive and negative triggers of specific metabolic states of individuals and populations” [61, 65, 95].
The previous reference was: [61,65].

“Systems biology approaches, including metabonomics, have emerged over the last two decades as a novel way forward to provide insights into the role of mammalian gut microbial metabolic interactions in individual susceptibility to health and disease outcomes” [95].
The previous reference was: [none].

“A series of investigations in human [74] and animal models [75–77] have provided a set of reference metabolic profiles of gut intestinal biopsies that can be used to assess not only compartment structure and function but also the gut microbial impact at the tissue level” [78, 95].
The previous reference was: [78].

"Such applications will help in identifying main metabolic processes conserved across species on which gut microbiota modulates to shape the microenvironment. For instance, the investigations illustrated how microbial-dependent variations along the upper intestine, an element often underestimated due to low bacterial populations, may affect utilization efficiency of dietary proteins and amino acids and their subsequent availability to extra-intestinal tissues. Moreover, some reference data were generated to investigate changes in gut functionality, such as gut permeability, using metabolic profiling of biofluids" [79, 80, 95].
The previous reference was: [78, 80].

"Both manifestations of IBD, ulcerative colitis (UC) and Crohn's disease (CD), are mediated by common and distinct mechanisms influenced by multiple environmental factors and specific genetic predispositions, including gut microbiota. Advancing knowledge regarding the mechanisms of IBD has led to the development of different therapeutic solutions based on surgery [82], cannabinoids [83], immunosuppression [84], and alternatively probiotic supplementation [85]. Although prognostic and monitoring tools are currently lacking, metabolic profiling in combination with state-of-the-art clinical and medical readouts is foreseen to be a valuable tool to differentiate and follow-up IBD evolution and response to disease-modifying interventions" [95]
The previous reference was: [none].

"Winterkamp et al. reported previously how N-methylhistamine, a key metabolite in mast cell metabolism involved in the pathogenesis of IBD, could be used as an indicator of disease activity in patients [86]. In this study, the urinary excretion of N-methylhistamine was associated with elevated histamine production and metabolism in CD and UC and could be used as a reliable diagnostic tool to monitor clinical and endoscopic disease activity in IBD. Additional proofs of concept on the feasibility to identify some metabolic indicators of early onsets of chronic inflammatory development offer also novel promising directions for patient monitoring and early patient stratification [87]. Additional applications of noninvasive profiling of stool from patients provided novel insights into the remodeling of the gut microbial communities and activities, concomitant to malabsorption and element of protein-losing enteropathy" [88, 89, 95].
The previous reference was: [88, 89].