System Biological Research on Food Quality for Personalised Nutrition and Health Using Foodomics Techniques: A Review

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Abstract Food quality is closely related to human health as people obtain energy from food. Traditional food science focuses on the provision of enough food for health guarantee. With economic development, people have a rising demand on quality and safety of the food they eat. Today, people are not only interested in eating sufficient and appropriate food, but expect to prevent diseases or treat existing diseases with diets. The development of the systems biology, especially various omics tools, is beneficial to the study of the impact of food compositions and ingredients on human health, advancing traditional food research into a new age: foodomics. Foodomics aims at studying the relationship between food quality and safety and food compositions and nutrition using omics tools such as genomics, transcriptomics, proteomics, and metabolomics, in addition to analytical techniques including chemometrics and bioinformatics. This review discusses recent advances in foodomics research.

Keywords: foodomics, food quality, food safety, nutrition, health

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1. Introduction

Food safety once has been, and remains undoubtedly a focus of attention of consumers. Nevertheless, with improvement of living standards, people nowadays have sufficient food to feed themselves and have higher requirements on food nutrition. People expect to know exact contents of their diets, and identify various foods that improve health and prevent possible diseases. Thus, a high requirement is imposed on food research improvement. Food constitutes a highly complex system, and traditional assessment instruments based upon analysis of constituents and components are ineluctably restricted by the factors such as the extraction methods. Moreover, from the perspective of food nutrition, emphasis on specific ingredients often leads to neglect of other ingredients or components that promote or impact health. Needless to say, study only on the effects of specific functional ingredients of food on specific metabolic pathways will also lead to neglect of the impact of food on the entire human body (Capozzi and Bordoni 2013). Foodomics has emerged as a new science with the increase of people's concern about food safety and food nutrients and the development of analysis techniques of high-throughput omics (genomics, transcriptomics, and metabolomics) in the postgenomic era (Capozzi and

Bordoni 2013). Additionally, the completion of genome sequencing of animals and plants that feed people has provided foundation for the application of various omics techniques.

The concept of foodomics first appeared in 2007 (N and I 2007, FoodOmics 2009). In 2009, professor Alejandro Cifuentes from the Institute of Food Science Research (CIAL) of the National Research Council of Spain first defined foodomics as a new discipline that studies the food and nutrition domains by using omics technologies, as reported in *Journal of chromatography A* (Cifuentes 2009). The goal of foodomics research is to improve consumers' well-being and health (Capozzi and Bordoni 2013, Herrero *et al.*, 2010, Herrero *et al.*, 2012, Cifuentes 2013). Therefore, the research objects of foodomics cover two domains: food science and nutrition science. By using a variety of omics techniques (e.g., nutrigenomics, microbial genomics, toxicogenomics, nutritranscriptomics, nutriproteomics, nutri-metabolomics, and systems biology), foodomics combines agricultural products, food compositions, and dietary structure with individual physical trait differences for health maintenance and disease prevention (Capozzi and Bordoni 2013). Subsequently, researches have been carried out on food quality, traceability, food safety and assessment, food ingredients and nutrition mechanism, ripening and food processing of post-harvest agricultural products, and

health-enhancement food products in relation with disease prevention.

The concept of foodomics is a natural result of food science development when the systems biology techniques are applied to the research of food nutrition and health. Since the completion of human genome project (HGP), scientists have conducted researches on the physiological and biochemical mechanisms in vital processes from the aspects of genes (including epigenome, single-nucleotide polymorphism (SNP), etc.), RNAs (including mRNAs, miRNAs, and LiRNAs), proteins, small molecule metabolites, and other aspects of the systems biology. Human health conditions are susceptible to genetic, environmental, and other factors, among which nutrients from people's diets are closely related to health. Food-related nutritional and health issues have become a major research direction in food science, and systems biology approaches become basic research tools. Moreover, food science is a comprehensive discipline that encompasses various subjects in different fields such as physics, biology, chemistry, and medical science. As a matter of fact, foodomics is the application of systems biology approaches in food science.

Soon after the concept of foodomics is proposed, numerous scientists who are specialized in fields related to foodomics quickly responded. Since 2009, International Conference on Foodomics has been held every two years in Italy, and the third conference was held (<http://foodomics.eu/>) in 2013. In 2012, the Electrophoresis magazine published a special issue on "Food analysis in the postgenomic era: Foodomics (Cifuentes 2012)," which elaborated the scope of researches and analysis approaches of foodomics. In November 2013, Prague of Czech Republic hosted the sixth international symposium on recent advances in food analysis, in which foodomics was listed as one of the thematic forums. In May 2013, the 10th International Conference of Food Science and Technology (ICFST) was held in Jiangnan University located in Wuxi of Jiangsu province in China, and foodomics was one of the 12 theme subjects under discussion.

The research methods and instruments of foodomics include food chemistry, analytical chemistry, biochemistry, molecular biology, food technology, and clinical science. With the purpose of enhancing the overall understanding of foodomics from different fields, this review gives a brief introduction to the scope of this research and analytical methods apart from the concept of foodomics.

2. Main Applications of Foodomics Researches

Two aspects in foodomics research are the food quality and safety and the relationship between food nutrition and health.

2.1. Food Quality and Safety Research

With economic development and trade globalization, food quality and safety issues start to draw global attention. Many nations are taking effort to boost research on food quality and safety not only in order to provide sufficient nourishing foods for consumers but also to

protect consumers from food fraud and drug and pesticide residue contamination. Foodomics facilitates systematic research on food quality and safety by including the compositions and quality of food, food discrimination and traceability, assessment of genetically modified foods, detection of food allergens, biotoxins, and other hazardous factors, impact of post-harvest storage and processing on active constituents of food into its research scope (Picariello *et al.*, 2012).

Food contamination detection and traceability/authentication. Foodomics greatly improves comprehensive analysis and research on food contaminants and allergens by identifying biomarkers for unsafe food so that unsafe food can be detected at an early stage to protect consumers. It can also facilitate establishment of more reliable approaches to food origin traceability and authentication. Nowadays, food components are various, and potential hazardous matters in food might differ tremendously. Traditional targeted analysis cannot detect contaminants and hazardous matters in food other than the target analyte. The metabolomics technique based on mass spectrometry provides a possibility of non-targeted analysis of hazardous matters. Mass spectrometry (MS) is so powerful that it can even detect unknown compounds and conduct structural analysis. What's more, it is easy to couple with highly efficient separation techniques such as gas chromatography (GC), high performance liquid chromatography (HPLC), and capillary electrophoresis (CE). Therefore, MS is a powerful instrument for analysis and identification of the total components in food, facilitating analysis of food quality and safety and origin traceability (Castro - Puyana *et al.*, 2013). For example, Tengstrand *et al.* utilized the electron impact time-of-flight mass spectrometry combined with ultra-high-pressure liquid chromatography (UHPLC-EI-TOF-MS) technique to identify the metabolic fingerprint of juice with various contaminants (Tengstrand *et al.*, 2013). By screening and selecting the peaks of abnormal compounds, they explored a new method of identifying unknown contaminants in juice. In the aspect of product authentication, many types of food have similar appearance but different nutritional values, which requires a developed food product authentication method. By utilizing high performance liquid chromatography/mass spectrometry (HPLC/MS), protein mass spectrometry and peptide fingerprinting of various foods can be analyzed, and specific peptide biomarkers can be screened based on rapid identification by HPLC coupled with multiple reaction monitoring mass spectrometry (Ortea *et al.*, 2012). Food allergens cause allergic reactions with people of specific groups. Specific food ingredients are fatal supposed that allergic reactions are severe. MS-based proteomics can effectively detect food allergens that are usually neglected by traditional nucleic acid detection or enzyme-linked immunosorbent assay (ELISA) based on antigen-antibody reactions. If the sample extraction process is optimized, traditional two-dimensional electrophoresis and protein microarray techniques will also be able to detect allergens as precisely as at the parts per billion (ppb) level (Picariello *et al.*, 2013). Because stable isotope mineral and mineral elements vary from one another in different regions, their fingerprint spectra can be built by employing stable isotope mass spectrometry and inductively coupled plasma

mass spectroscopy (ICP-MS). This can then be used in food origin traceability and identification of animals and plants from different origins (Zhao *et al.*, 2014).

Monitoring and appraisal of production and processing of foods. An increasing number of different organic food products are present in the market, providing consumers with a variety of choices. Organic foods are produced in different ways from traditional foods, in terms of pesticide and veterinary drug residues and nutritional components. Therefore, traditional food analysis methods such as targeted detection are no longer capable of authenticating organic food products to ensure food quality. By utilizing proteomics and metabolomics, researchers can comprehensively compare organic and traditional food products on the molecular level and quickly identify organic food products in clusters (D'Alessandro and Zolla 2012). People rely on animal-derived foods such as meat, milk, and eggs as their main sources of dietary proteins. Animal-derived foods are susceptible to quality damage and putrefaction during food processing, storage, and transportation. Therefore, quality and safety monitoring of these foods is of remarkable significance. Proteomics and metabolomics instruments can be used to analyze the protein components and composition changes during processing, storage, and transportation of these products, in addition to identifying proteins and small molecular markers related to food quality. In this way, potential adulteration, food putrefaction, and other food safety problems can be identified (Cozzolino *et al.*, 2002, Gaso-Sokac *et al.*, 2010, Gaso-Sokac *et al.*, 2011, Leitner *et al.*, 2006). Similarly, the foodomics technologies including proteomics and metabolomics can be utilized in authenticating and analyzing chilled fresh meat and refrigerated meat. Protein compositions and metabolite changes of post-slaughter animal meat can also be studied to enhance meat product quality and prolong shelf-life (D'Alessandro and Zolla 2013). Traditional fermented food products are prone to safety risks due to their special manufacturing procedures. Fast identification of specific small molecular matters produced in the enzyme fermentation procedures of these foods can be achieved using metabolomics techniques. Then, these markers can be used for quality control of these fermented foods with metabolic fingerprints built up (Hannon *et al.*, 2007). In the 2013 Recent Advances in Food Analysis (RAFA) conference, Clementine Le Boucher from the French Academy of Agricultural Sciences reported "Toward new comprehension of cheese ripening." Using GC/MS and fingerprint analysis techniques, the authors compared various cheeses prepared with different fermentation time and found 45 different metabolites (12 amino acids, 25 volatile constituents, 4 vitamins, and 1 carnitine) along with unknown constituents by omics studies. The study provides indicators for assessing various types of cheeses with different ripening levels or different flavors. Moreover, metabolomics can be applied to the research of physiological changes in post-harvest fruits and vegetables, providing theoretical foundation for the research of preservation and control technologies of fruits and vegetables (Ibanez *et al.*, 2012).

Agricultural products improvement and genetically modified foods. Applying systems biology approaches in the research of food sources (i.e. animals, plants, and

crops) to enhance the planting and breeding technologies so as to increase productivity and promote quality is indubitably significant for food safety improvement. For instance, flatfish is extensively cultivated for its appreciable nutritional and commercial values. During the metamorphosis period when flounder larvae turn into benthic, flatfish often dies from fatal diseases such as pathological changes of fishbone and pigmentation deposition. Therefore, the transcriptomics study of flatfish is necessary in order to comprehensively understand the physiological and biochemical processes of reproduction, growth and development, nutrition supply, and immunology, etc. Study on the nutritional needs of flounder larvae in the process of metamorphosis and the nutrients' impacts on its development and growth is notably important. Better cultivation techniques and feeding formulas can be derived to enhance the flatfish quality and its nutritional value (Cerdeira and Manchado 2013, Murray *et al.*, 2010). MiRNAs regulate gene expression of organisms in vivo. Fu *et al.* conducted study on the changes of miRNA expression of flounder larvae during metamorphosis by the RNA sequencing technology and discovered miRNAs specific to pigmentation deposition and deformation. This is massively significant on the exploration of the regulatory network of gene expression during the process of metamorphosis (Fu *et al.*, 2011). Genetically modified foods have always been under dispute from the beginning. Backlash from consumers and potential hazardous effects lead to various restriction policies on the research, production, and sale of genetically modified foods in all countries. Therefore, comprehensive evaluation of transgenic products becomes urgent and increasingly important. However, no single traditional research method is able to implement comprehensive assessment on the impacts of genetically modified food on human health and environment. Instead, foodomics analysis techniques are able to comprehensively analyze the compositions of genetically modified food on the levels of transcriptomics, proteomics, and metabolomics. In the meantime, this study combines bioinformatics and chemometrics methods to contribute to the research on potential biological effects of genetically modified products (Valdés *et al.*, 2013). An increasing number of metabolomics and proteomics techniques based on mass spectrometry are utilized in the analysis of genetically modified foods (Agrawal *et al.*, 2013, Garcia-Canas *et al.*, 2011, Valdés and García - Cañas 2013). Cifuentes *et al.* (Simo *et al.*, 2010) applied the CE-TOF-MS technique to the analysis of more than 150 proteolytic peptides for both transgenic soybeans and traditional soybeans, but no significant difference was found. This study sheds light on new assessment methods for the safety of genetically modified food on the proteomics level.

2.2. Research on the Relationship between Food Nutrition and Human Health

Human physical health is determined by both genes and the environment, and food intake is the most crucial external factor for human health. After being consumed, food alters human body gene expressions as well as the protein and metabolite composition levels, and different food ingredients would lead to different alterations. Due to

genetic differences of each individual, human reacts with food ingredients differently. In this situation, the application of foodomics techniques is very important to the analysis of the impacts of food compositions on genomes, transcriptomes, proteomes, and metabolomes. This is because researches on food and nutritional mechanisms at the molecular level to define the correlation of the genes and diets with health will elucidate the optimization of the design on dietary compositions and regulation of human physiological state as well as the development of health-enhancing functional food and disease prevention (Corella *et al.*, 2011). As a result, nutritional values of food to human health will become a research focus of food science following food quality and safety.

Food compositions and their impacts on physiological health. Food influences human health as a major source of human nutrition, and therefore researches on various food compositions and their influence on physiological health have significant effects on the prevention of diseases by means of optimized daily diet, especially identification of risky and hazardous factors in food and functional components favorable to disease prevention and treatment. These researches mainly focus on the functional mechanism of active components in food on human health at the levels of proteomes, genomes, and metabolomes (Corella *et al.*, 2011, Wittwer *et al.*, 2011). For example, during the course of aging, accumulation of in vivo oxidative stresses will cause diseases such as diabetes, atherosclerosis, neurodegenerative diseases, and other inflammation diseases because in vivo oxidative stresses trigger post-translational modifications in proteins, mostly carbonyl modifications. Research results in recent years demonstrated that antioxidative components in daily diet could distinctly reduce protein oxidation in human bodies, thus ameliorating the state of oxidative stress. Antioxidants differ in their abilities to ameliorate oxidation of different proteins at different binding sites, and therefore quantitative assessment of the amelioration effects of various antioxidants on different protein oxidation at the protein level will help improve the diet pattern for disease prevention and deferment of senescence (Madian *et al.*, 2013). Valdes *et al.* applied transcriptomics and metabolomics strategies to the study of the anti-proliferative effects of dietary polyphenols extracted from rosemary on two human leukemia lines, with one being drug-sensitive (K562) and the other being drug-resistant (K562/R) (Valdes *et al.*, 2012). Microarray techniques were used for transcriptomics analysis and MS-based non-targeted analytical approaches (CE-TOF MS and UPLC-TOF MS) were used for metabolomics analysis. With the combined studies of transcriptomics and metabolomics, it was found that rosemary extracts had different functional mechanisms on the two phenotypes of leukemia lines. In addition, ingenuity pathway analysis (IPA) was used as a bioinformatic tool to study the gene changes to find out the genes that lead to different metabolic pathways of two human leukemia lines, providing the inhibitory mechanism of leukemia cell proliferation from rosemary extracts. Then, Valdes *et al.* first researched the bioactivity of rosemary extracts against colon cancer cells at the molecular level via the foodomics methodology based on the combined analytical platforms of transcriptomics, proteomics, and

metabolomics studies (Ibanez *et al.*, 2012). This allows determination of changed genes, proteins, and metabolites that are correlated with antioxidation, pro-apoptosis, and cell proliferation inhibition, which provides new insights on the establishment of the biological mechanisms of rosemary extracts with biological data. Red microalgae contain a variety of functional constituents such as sulfated polysaccharides, polyunsaturated fatty acids, zeaxanthin, vitamins, minerals, and proteins. After red microalgae products were fed to mice, it was found that the products significantly improved the total serum cholesterol, serum triglycerides, hepatic cholesterol levels, and HDL/LDL ratios, and increased excretion of neutral sterols and bile acids. These findings support the possible usage of red microalgae as novel nutraceuticals (Dvir *et al.*, 2009). In the meantime, based on the relationships between food components and diseases, the proteomics technology can be used to characterize and screen food allergens so as to prevent health hazards (Picariello *et al.*, 2013).

Research on individual nutrigenetics. Many diseases and unhealthy status, such as obesity, diabetes, mellitus and cardiovascular diseases, and cancers, are closely related to human diet. Moreover, these diseases and human's susceptibility to these diseases are correlated with a variety of gene mutations. With the completion of the human genome project and subsequent sequencing, the relationship between genetic heterogeneity and human health is gaining attention. Responses to such individual genotype differences by adjusting people's diet to safeguard human health will be a research focus of future food science (Williams *et al.*, 2008). For example, the polymorphism of apolipoprotein A-II (APOA2) promoter subregion (-265T > C) is associated with lipid metabolism and obesity. Individuals with the CC gene type are likely to be more obese than those with the TT or TC gene type. The total fat and protein intake is statistically higher in CC gene type individuals than in TT or TC gene type individuals. Therefore, regulating dietary intake of these people will help reduce obesity (Corella *et al.*, 2007). Valdes *et al.* utilized transcriptomics techniques to study the effects of rosemary extracts on the transcriptional gene changes of human colon cancer cells SW480 and HT29 and found only 18% of the differentially expressed genes were common in both cell lines, indicating that the two lines of human colon cancer cells (SW480 and HT29) caused by different gene mutation had different reactions with the same active component (Valdes *et al.*, 2013). Based on this, the authors utilized two bioinformatics tools (i.e. Ingenuity Pathway Analysis and Gene Set Enrichment Analysis) to carry out functional analysis on the mutated genes to deduce the possible signaling pathway of inhibition of cell cycles and apoptosis caused by rosemary polyphenols.

3. Development on Foodomics Technologies

It is not difficult to conclude from the previously mentioned concept of foodomics that the analysis techniques of foodomics are common omics techniques used in the systems biology, such as genomics, transcriptomics, proteomics, and metabolomics. Each

technique produces huge amount of data, and as a result, bioinformatics and chemometrics developed along with the omics are becoming indispensable tools of foodomics research.

3.1. Genomics Techniques

Food nutrition and human genes are highly correlated as human bodies are exposed to food every day. In this case, human health is a result of interaction between genes and exposure to environments including food. Therefore, the association of food nutrition with health is difficult to investigate without genomics researches. Researches on the relationships among genes, diet, and health are based on the researches of the functional mechanism of food nutrition at the molecular level. Genomics studies in foodomics can be conducted in two aspects (Capozzi and Bordoni 2013). On one hand, genomics studies have shown that human diseases and human's susceptibility to certain diseases are related to various gene mutations. Human's susceptibility to certain diseases can be adjusted by proper diet regulations. Therefore, investigating different responses of structural or functional genomes to food and analyzing the relationships between nutrient components and health and diseases could greatly accelerate individual nutrigenomic study and appropriate alterations of the diet plan for certain people (Wittwer *et al.*, 2011). On the other hand, applications of genomics techniques to the promotion of agricultural product quality, especially nutritional components of bulk agricultural products, may provide a solution to malnutrition and some other diseases (Pérez-Massot *et al.*, 2013). Genomics technologies can be categorized into microarray and genome sequencing techniques. The former mainly determines and assesses the differences of genomes in each individual using various gene chips (e.g., sequencing chips, single nucleotide polymorphism chip, methylation chip, copy-number chip, and molecular cytogenetic chip) designed with known genomic information; the latter is the main next-generation sequencing technology (e.g., De novo genome sequencing, resequencing, and RNA sequencing) that is still being studied today (Cerdeira and Manchado 2013).

3.2. Transcriptomics Techniques

The transcriptomics technology covers the whole set of gene expressions in a sample, usually the full expression of mRNAs. The adjustment functionality of non-coding RNAs in gene expression is drawing growing attention today, and miRNAs, LncRNAs, and other RNAs are also the major targets of the transcriptomic research. The research on the mRNA expression levels reflects the impact of food on gene expression regulation, because gene expression regulation has a significant relationship with human health status. Therefore, the transcriptomics technology can be applied in the research on the role of active food components in the maintenance of physiological equilibrium and disease prevention (Bordoni *et al.*, 2007). Similar to the genomics technology, the transcriptomics technology also includes two types of techniques: microarray and sequencing. Currently, many companies such as Agilent, Illumina, and Affymetrix have developed mRNA and miRNA gene expression chips of various species including humans'. Companies in China

such as CapitalBio (Beijing) have also developed a variety of mRNA expression profiling chips and have integrated the LncRNA detection probe into the chips, which can be utilized in expression profile measurement of mRNAs and LncRNAs of various species. With the development of the sequencing technology and reduction of its price, sequencing assessment of all the mRNA, miRNA, and LncRNA expressions in human bodies (in vivo) with the transcriptomics technology becomes possible for those species without expression profiling chips.

3.3. Proteomics Techniques

Proteomic technologies are applied to the analysis of the total protein compositional data in a sample. Protein compositions in food are closely related to food quality issues such as food safety, origin, category, and processing. Even food with extreme genetic homogeneity may have different functions and components. Neither genomics nor transcriptomics can truly reflect protein compositions and variations in food because of the post-translational modification process of proteins. Therefore, food analysis at the proteomic level has significant importance in enhancing food quality and safety (D'Alessandro and Zolla 2012, Agrawal *et al.*, 2013, Boschetti and Righetti 2012). Meanwhile, analysis on proteomic changes of human cells or tissues after food is taken into human bodies will help study the mechanism of food nutrition and its relationship with health. It will also address such challenges as to determine active substances in food for prevention of cancers and other diseases (Shukla and George 2011). A variety of proteins exist in biological samples with a magnitude of concentration differentiation, and many trace proteins provide important functions for the samples with the concentration levels below the detection sensitivity. Therefore, various protein isolation and identification technologies are needed and the isolation and separation of a large quantity of protein samples is the basis of proteomics research. The traditional two-dimensional polyacrylamide gel electrophoresis (2-DE) method is extremely time-consuming and tedious, and it has a lot of constraints in isolation of tremendously-high molecular weight proteins, particularly-low molecular weight proteins, extremely alkaline proteins, and hydrophobic protein. In order to reduce the complexity of samples, protein isolation is applied in proteomics research using multi-dimensional liquid chromatography, which gradually becomes a major technology. Mass spectrometry including various TOF-MS techniques is currently a major method for protein identification after protein isolation. Generally, two proteomics analysis strategies are used before mass spectrometry. One is the "Bottom-up" strategy, by which the "Shotgun" approach first performs protein enzymolysis and then uses chromatography to isolate and purify the resulting peptides for subsequent mass spectrometry. The other is the "Top-down" strategy, where the protein samples first go through chromatography and then enzymolysis to generate peptides, and finally mass spectrometry is carried out on the peptides. The former method is easily automated and suitable for a large quantity of protein identification; the latter is suitable for analysis of a post-translational modification site. The protein chip technology developed

based on microarray has also been applied in proteomics analysis. The recently developed lab-on-a-chip system (or Micro Total Analysis System) assembles all the protein extraction, separation, and identification processes on one microfluidic chip. In this way, the efficiency of the proteomics analysis is greatly increased by reduced sample consumption, analysis time, and cost (Nazzaro *et al.*, 2012).

3.4. Metabolomics Techniques

Metabolomics studies all endogenous or exogenous small molecule metabolites with a molecular weight less than 1000 D in a biological system and explores their metabolic pathways. The metabolome represents the final phenotype of a genome and is the terminal of various reaction processes in the biological systems. Studies of metabolic phenotypes and metabolic mechanisms help us to differentiate different metabolite pathways of food components in human bodies and to view their metabolic composition changes. We can also use metabolomics to analyze different impacts on physiological functions of various metabolites. After analyzing the physiological health state, we could find metabolic markers related to health status and food nutrition so as to evaluate the nutritional functionality of food (Villaño *et al.*, 2013). Besides the study of food-induced metabolic changes in human bodies, metabolomic studies also include the study on the compositions of large-scale small molecule metabolites in food, analysis and assessment of active functional components or hazardous ingredients of food, which could help discriminate food quality and identify food sources by fingerprint chromatography of food metabolites. Huge quantities of small-molecular substances exist in food and human bodies, which possess different physicochemical attributes and have different concentrations, bringing challenges to metabolomic analysis techniques. Currently, metabolomics techniques are mainly classified into mass spectrometry (MS) and nuclear magnetic resonance (NMR) techniques (Hu and Xu 2013). These two techniques are separately used in combination with sample separation techniques such as liquid chromatography (LC), gas chromatography (GC), and capillary electrophoresis (CE) (Scherer *et al.*, 2013). According to the study purpose, these researches can be divided into metabolic target analysis for one or several kinds of specific biomarkers, metabolomic profiling for a group of metabolites with the same metabolic pathway or other characteristics, and metabolic fingerprinting for different metabolic phenotypes in response to different cellular environments. Inoue *et al.* applied UPLC-FL-ESI-TOF/MS in combination with fluorescence derivatization to establish a platform for identifying active compounds with unknown functionalities in food (Inoue *et al.*, 2013). CE is a foodomics technique commonly applied in the analysis of food components, which is often used with MS for the analysis of amino acids, bio-amines, proteins, peptides, nucleic acids, carbohydrates, phenols, pigments, toxins, pesticides, vitamins, additives, and organic and non-organic ions in food as well as food processing procedures. CE is utilized in the surveillance of food quality, safety, nutritional values, and processing and transportation procedures (Ibáñez *et al.*, 2013). Review articles are published each year on "electrophoresis" to

introduce this method and its application (Herrero *et al.*, 2010, García - Cañas *et al.*, 2014, Castro-Puyana *et al.*, 2012). Çelebier *et al.* described the detailed procedure of CE on the research of the changes of metabolites under the effect of rosemary extracts on colonic cancer cells HT29 using the CE-MS technique (Celebier *et al.*, 2012). A research conducted by Vazquez-Fresno *et al.* demonstrated that hydrogen nuclear magnetic resonance spectroscopy could be utilized in obtaining grape wine metabolite profiles in human urine and in detecting endogenous physiological markers after grape wine drinking (Vazquez-Fresno *et al.*, 2012).

3.5. Other Omics Techniques

The significance of foodomics lies in that it provides omics-based research ideas. To enhance the pertinence of studies, facilitate data analysis, and clarify the mechanisms, different researches on various levels of omics can be carried out for different foods and research objects. To study the mechanism of food components influencing human health, more special omics, such as epigenome, non-coding RNAomics, and post-translated modification proteome and enzymome, recently emerged and were applied as foodomics techniques (Gaso-Sokac *et al.*, 2010). For example, the epigenome technology mainly focuses on non-sequence changes of DNAs (which majorly includes DNA-methylation, histone modification, and non-coding RNAs including small RNAs). In mammals, many food components such as folic acid, vitamin B6, vitamin B12, betaine, methionine, and choline are found in relation with DNA-methylation. By analyzing epigenome alterations induced by food components, researches on food nutrients and their relationships with disease prevention can be carried out (Cifuentes 2013). Epigenomics analysis techniques majorly comprise chromatin immuno-precipitation DNA sequencing. In quality control and safety analysis of food, more precise subdivisions of omics, such as peptidome, lipidome (Wang and Zhang 2011), glycome, polyphenols (Delcambre and Saucier 2013, Picariello *et al.*, 2012), and enzymome (Josic and Giacometti 2013), appear to aim at different components and ingredients in food. After the special components that represent the specific physiological state of food are analyzed, the storage and processing (freezing and thawing) of food can be properly monitored.

3.6. Chemometrics and Bioinformatics

A variety of foods and their composition complexity impose high requirements on food analysis or experimental design. In addition, the application of modern foodomics techniques definitely generates a large amount of complex experimental data. Therefore, one of the challenges in foodomics is to appropriately design experiments, analyze measurement data, and obtain useful information from the data (Erazo *et al.*, 2013). Chemometrics and bioinformatics are two important tools for data analysis in foodomics. Developed on the basis of chemistry, chemometrics incorporates the theories and methods of mathematics, statistics, computer science, and other related studies into chemical analysis, optimizes experimental design, and acquires complicated relationships between chemical compounds, structures,

and performance to the greatest extent using measurement data based on analytical chemistry (Skov and Engelsen 2013). Currently, the common chemometric methods used in food analysis include principal component analysis (PCA), discriminant analysis (DA), clustering analysis (CA), partial least square regression (PLS), multiple linear regression (MLR), artificial neural network (ANN), soft independent modeling of class analogy (SIMCA), and wavelet transform. When combined with techniques such as infrared spectroscopy (IR) and GC-MS, these chemometric techniques can be applied to food nutrient analysis and nutrient monitoring during food production and processing (Ammor *et al.*, 2009, Xie *et al.*, 2009, Jalali-Heravi *et al.*, 2006). For example, Mohammed *et al.* proposed a method for rapid monitoring of the spoilage of minced beef using Fourier transform infrared spectroscopy in tandem with chemometrics (Ammor *et al.*, 2009). Food nutrient analysis techniques combining chemometrics with GC-MS can also be utilized to detect adulterants in edible oils and foods (Zhu *et al.*, 2010, Vlachos *et al.*, 2006).

Unlike chemometrics, bioinformatics is used to explore the correlations between food nutrition and health. By processing mass data of genes, proteins, and metabolites measured by foodomics, bioinformatics is used to discover the relationships between specific data and human physical health. Currently, most of the researches on the mechanism of food compositions in human bodies using the techniques of transcriptomics, proteomics, and metabolomics have large amount of descriptive data (Wittwer *et al.*, 2011). Since little has been known about the functions of most genes, proteins, and metabolites, in order to explain and elaborate these data, bioinformatics provides a tool for possible molecular signal transfer in a wide range from food compositions to impacts on health. A variety of bioinformatic tools have been developed and used for functional annotation and clustering of genes and proteins generated via omics techniques. Using statistics, the potential biomarkers of food nutrition and health can be discriminated; with the knowledge of signaling pathways, potent nutritional molecular mechanisms can be evaluated. For instance, Valdes *et al.* used two bioinformatics tools Ingenuity Pathway Analysis and Gene Set Enrichment Analysis to analyze the data of transcriptomics, proteomics, and metabolomics after rosemary extracts were applied to cancer cells and analyzed the mechanisms of rosemary by giving possible signaling pathways (Ibanez *et al.*, 2012, Valdes *et al.*, 2012, Valdes *et al.*, 2013). In the RAFA conference in 2013, Lieven van Meulebroek *et al.* from Ghent University in Belgium reported the research results on the regulation of plant hormones generated by the carotene metabolism in tomatoes based on foodomics. The results were obtained by using UPLC-Orbitrap and related bioinformatics tools Sievetm (fingerprinting analysis) and Simcatm (data processing). The development of bioinformatics facilitates data analysis and explanation, and in return the bioinformatics is developed based on data analysis. In this regard, after data analysis is complete and some explanations are given using bioinformatics, the results need to be verified with traditional chemical or biological experiments.

4. Conclusions

The systems biology and its development in the fields of life science, medical science, and pharmacology provide boundless opportunities and challenges for food nutrition and health studies. These subjects are associated with food science and gradually become key directions for future research on food science. Cardiovascular diseases, diabetes, and cancers, which are developed by the joint action of the living environment and genes, are becoming major threats to human health in a modern society. Food, as the external environmental stimulus that is correlated with people in their lifetime, is closely related to the occurrence and development of these diseases. Therefore, based on the traditional concepts of sufficient feeding and good feeding conditions, food science has been further developed into a new era when people have higher requirements on food science, including food nutrition and health research at the systems biology level and based on personalized diet for maintenance of good health. In this manner, pains brought by body diseases can be mitigated, a large sum of medical costs can be saved, and the happiness status brought by foodomics can be achieved. In addition, researches on foodomics require cooperation of people working in different fields such as food science, analytical chemistry, clinical science, pharmacology, and life science. Subsequently, foodomics will greatly accelerate our researches on food safety, traceability, quality, new foods, transgenic foods, functional foods, and nutraceuticals.

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