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Omics analysis in nutrition science

Las ómicas en la nutrición

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Abstract:

The prevalence of diseases affecting human health related to the environment and inadequate nutrition is high. Strategies that seek to mitigate them have focused on lifestyle changes and healthy nutrition focusing on general guidelines that do not benefit all individuals. Therefore, new omics approaches have been proposed. The word "omics" is used as a suffix in molecular biology and consists of the study, quantification, identification and characterization of the whole or a set of molecules involved in the structure, function and dynamics of a cell, tissue or organism. Mainly genomics, epigenomics, transcriptomics, proteomics and metabolomics. In this regard, human nutriomics combines food sciences with omics focused on the genome of each individual, in order to take advantage of interindividuality to promote nutritional strategies that prevent, manage and treat diseases and optimize health. However, these novel tools present challenges when implementing them and interpreting their results, so it is recommended to continue conducting research in the area and training in the management of techniques and interpretation of results for the full exploitation of nutrition in the future. This article aims at providing health professionals with general information on the different omics approaches involved in nutritional sciences in order to elucidate the molecular mechanisms focused on personalized nutrition.

Keywords:

Nutrigenomics, epigenetic, proteomic, personalized nutrition, metabolomic, transcriptomic, human nutriomics

Resumen:

La prevalencia de las enfermedades que afectan a la salud humana relacionadas con el medio ambiente y una inadecuada alimentación es alta. Las estrategias que buscan mitigarlas se han centrado en cambios en el estilo de vida y una nutrición saludable enfocándose en pautas generales que no benefician a todos los individuos. Por tanto, se han propuesto nuevos enfoques ómicos. La palabra "ómica" es utilizada como sufijo en biología molecular y consiste en el estudio, cuantificación, identificación y caracterización de la totalidad o de un conjunto de moléculas involucradas en la estructura, función y dinámica de una célula, tejido u organismo. Principalmente se encuentran la genómica, la epigenómica, la transcriptómica, la proteómica y la metabolómica. Al respecto surge la nutriómica humana que combina las ciencias de los alimentos con las ómicas centradas en el genoma de cada individuo, con el fin que con el aprovechamiento de la interindividualidad impulsar estrategias de nutrición que prevengan manejen y traten enfermedades optimizando la salud. Sin embargo, éstas novedosas herramientas presentan desafios al momento de implementarlas e interpretar sus resultados por lo que se recomienda continuar realizando investigaciones en el área y capacitándose en el manejo de las técnicas e interpretación de resultados para el completo aprovechamiento de la nutrición en el futuro. Este artículo tiene como objetivo proporcionar de manera general a los profesionales de la salud información sobre los diferentes abordajes ómicos implicados en la ciencias de la nutrición con el fin de dilucidar los mecanismos moleculares enfocados en una nutrición personalizada.

Palabras Clave:

Nutrigenómica, epigenetica, proteómica, nutrición personalizada, metabolómica, transcriptómica, nutriómica humana

INTRODUCTION

The environment and inadequate dietary intake have been considered the main factors affecting human health and causing various diseases in the individual.[1] Programs focused on lifestyle changes are based on general guidelines for healthy nutrition and physical activity. However, approximately 30% of participants do not respond or adhere to the intervention, so elucidating the molecular mechanisms by which such interventions have not had the expected effect would provide valuable tools, yielding better results in interventions and making them more effective using personalized nutrition. Such nutrition is defined by the American

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Dietetic Association as: "A field that harnesses human individuality to drive nutrition strategies that prevent, manage and treat disease while optimizing health".[2,3]

The word "omics" is used as a suffix in molecular biology and is the study of the whole or a set of molecules. Thus, omics sciences refer to a field of study of biological sciences, which are grouped according to the suffix "-ome" and aim to identify, characterize and quantify all biological molecules that are involved in the structure, function and dynamics of a cell, tissue or organism.[4] These sciences use biotechnology to isolate and characterize a large number of biomolecules from the same group such as DNA, RNA, proteins or metabolites.[5] Among the main omics are: genomics, transcriptomics, epigenomics, proteomics and metabolomics, serving as novel tools. In this sense, human nutriomics is considered a new discipline formed from the combination of food sciences and omics focused on the gene of each individual achieving a personalized nutrition, which are integrated with massive analysis in order to provide a personalized nutritional guidance that yields better results.[6,7]

GENOMICS

After the Human Genome Project, new knowledge about the influence of nutrients in people's diets was postulated as a gene-nutrient interaction that would lead to the pre-description of specific diets for each individual, and nutrigenomics was introduced.[8] Nutrigenomics is, therefore, the area of nutrition that uses molecular tools to understand the various responses as a function of an inter-individually applied diet based on gene sequence, as exemplified in Figure 1.[1] This science seeks to elucidate how the components of a particular diet affect the expression of genes, either by increasing their potential or suppressing them, depending on whether these genes show a modified activity or an alteration in their expression.[9]

Nutritional genomics generally uses genome-wide association studies (GWAS), which aim at identifying associations of genotypes with phenotypes by analyzing differences in the allele frequency of genetic variants between individuals that are ancestrally similar but phenotypically different.[10] These studies have found several genetic variants associated with specific nutrition-related traits, such as nutrient absorption and utilization, lipid metabolism, fat accumulation, and gene-diet interactions, as well as diseases, such as obesity and cardiovascular disease.[11] These studies have also identified loci associated, that is to say, specific locations on the chromosome where specific genes or variants in specific genes are located, associated with various genotypic traits. Some outstanding examples for personalized nutrition are given in SNV (single nucleotide variant), formerly called SNP (single nucleotide polymorphisms), related to the metabolism of macro and micronutrient intake, cholesterol metabolism, obesity, fasting blood glucose, etc.[12]

An example of disease-associated GWAS has been linked to type 2 diabetes, where common variations were shown to explain approximately 20% of the overall risk for developing type 2 diabetes, an analysis of common SNPs identified three loci associated in the non-coding regions near *CDKN2A* and *CDKN2B*, as well as replication associations near *HHEX* and *SLC30A8*.[13,14] In relation to obesity, among the most studied genes related to the risk of developing obesity is the *FTO* (fat mass and obesity-associated) gene, in which the presence of variants rs9939609/A related to diets high in lipids and rs8050136/A related to diets high in carbohydrates were found with greater susceptibility to obesity.[15]

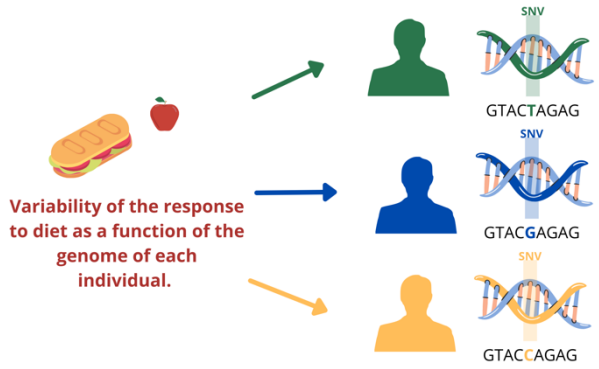

Figure 1. Association between diet and health with a nutrigenomic approach.[1,8,9]

EPIGENOMICS

The concept of epigenetics refers to the control of gene expression by mechanisms that are not directly related to the DNA coding sequence.[16] Epigenetics is information transmitted based on gene expression through various epigenetic marks (chemical compounds added to DNA or histones) that are recognized by enzymes that deposit or remove the specific mark. These marks change the chromatin information by either preventing the binding of transcription factors to the DNA by compacting it or allowing the binding of these factors by opening it and generally up-regulating cellular processes. Such changes begin slowly and are progressive and potentially reversible.[17] DNA methylation acts at promoters to drive gene silencing, leading to inhibition of transcription or maintenance of the repressive state of chromatin and acetylation of histones unwinding chromatin.[18]

Nutrition is among the most studied factors that modify the epigenome, where several associations have been observed between adverse prenatal nutritional conditions, postnatal health and increased risk of disease. For example, in humans, there are epigenetic differences associated with prenatal exposure to caloric restriction, which have been attributed to a lower degree of methylation of a gene involved in insulin metabolism than those not exposed.[19] Regarding colorectal and pancreatic cancer, low folate intake has been associated with hypomethylation and

an increased risk of developing this type of cancer.[20] Respecting prediabetes and obesity a study in mice showed that an obesogenic diet led to epigenomic modifications in the liver that alter gene regulatory networks associated with epigenomic changes.[21]

TRANSCRIPTOMICS

Transcriptomics studies the set of activated RNA transcripts. The mRNAs are produced at a specific time and tissue of a selected organism, so gene expression is variable depending on the different circumstances and time periods.[5,22] Transcriptome analysis can evaluate the expression of thousands of genes before and after interventions, helping to establish new diagnostic biomarkers of disease between healthy and diseased individuals. An example of the above has been seen in diabetic retinopathy, where commonly employed diagnostic biomarkers include those related to retinal vasculature (endothelin-1, nitric oxide-related, ADMA), measures of blood glucose (HbA1c), lipids (ApoA1, ApoB, AGE-LDL), inflammation (WCC, ESR, CRP, cytokines, chemokines, transcription factors), angiogenesis (VEGF, PEDF, FGF-21), among others, have contributed to the development of new therapies particularly in late stages. However, many patients with this pathology do not respond adequately to current treatments, so more effective treatments are recommended. Biomarkers can help to better understand the disease and therefore contribute to the development of new strategies and clinical treatments to prevent vision loss in people with diabetes.[23] A recent study determined differential gene expression in response to elevated glucose in lymphoblastoid cell lines from individuals with diabetes with and without retinopathy identifying folliculin gene activity (*FLCN*) as a susceptibility gene for diabetic retinopathy as a potential new biomarker for the disease.[24]

Likewise, with respect to nutrition, the consumption of macro and micronutrients contributes to gene expression, altering metabolism and the development of disease. This type of analysis can also evaluate the expression of thousands of genes before and after dietary intervention, helping to establish new diagnostic biomarkers.[25] For example, one study conducted an intervention by administering a traditional Mediterranean diet, found differences in the gene expression profile in subjects following the Mediterranean diet compared to control subjects and showed that one of the mechanisms by which the Mediterranean diet, particularly rich in virgin olive oil, may exert health benefits is through changes in the transcriptomic response of genes (n=241) related to cardiovascular risk.[26]

For the study of transcriptomics it is necessary to study the cells in which genes are expressed in specific tissues, due to the difficult access in human tissues, the samples that are regularly available are from subcutaneous adipose tissue, blood mononuclear cells and skeletal muscle.[27]

This type of analysis can also help by identifying proteins, genes or metabolites that change in the pre-disease state and characterize pathways regulated by either nutrients or bioactive compounds present in foods.[5,8,22]

METABOLOMICS

Metabolomics studies metabolites in human systems, particularly changes in biochemical profile, blood, urine, saliva, cells and tissues. Such studies are able to evaluate a group of metabolites associated with a particular metabolic pathway or compare changes in metabolite patterns in response to environmental stimulants, thus considering the outcome of the human molecular analysis, being able to evaluate at this point the body's response to a specific diet if nutrition is to be targeted.[28] In this sense, this contributes to the understanding of how the excess or absence of nutrients or secondary metabolites present in foods may affect the health/illness of each individual by changing the metabolome pathways in the body.[29]

Metabolomic studies have identified metabolites associated with the development of type 2 diabetes in humans, identifying around 50 to 80 metabolites characterized by a state of insulin resistance or fully developed diabetes, which are amino acids and intermediates of their degradation pathways followed by lipids mainly phospholipids/lysophostide.[30] Likewise, metabolomics has also proven useful in identifying new biomarkers of cardiometabolic diseases and detecting future events, interventions and new insights into the biological pathways that contribute to the development of diseases.[31]

PROTEOMICS

Proteomics studies the complete group of proteins of the whole organism, which are involved in the biological processes of a particular species. It analyzes a protein that is being expressed during a specific time, it is considered the most accurate method to establish the effects of nutrients and food components on the genome.[32]

A recent study evaluated the cross-sectional association of proteomic, metabolomic and serum markers with three dietary patterns: Alternative Healthy Eating Index (AHEI), Dietary Approaches to Stop Hypertension (DASH) diet and a Mediterranean diet (MDS) using data from patients participating in the Offspring Study who had proteomic (n=1,713) and metabolomic (n=2,284) data. Food frequency questionnaires were used to derive dietary pattern indices, then multivariable adjusted linear regression models were used to relate each dietary pattern index to each proteomic and metabolomic marker. As a result of the 1373 proteins they found 103 were associated with at least one dietary pattern (40 with AHEI, 83 with DASH and 8 with MDS). The results of the proteins that were found to be significant were enriched in biological

pathways involved in cellular metabolism/proliferation and immune response/inflammation. The authors suggested that proteins and metabolites associated with the resulting dietary patterns may help characterize intermediate phenotypes that yield insights into molecular mechanisms involved in diet-related diseases.[33]

PERSONALIZED NUTRITION

Personalized nutrition is growing rapidly, tailoring dietary recommendations to specific biological needs based on the patient's health status and goals. For example, the metabolic disease known as phenylketonuria is caused by a loss-of-function mutation of the phenylalanine hydroxylase (*PAH*) gene resulting in the accumulation of phenylalanine that can lead to organ damage, neurobehavioral abnormalities and mental retardation. When this disease is detected, a strict control of phenylalanine intake is performed with a sufficient supply of tyrosine, giving a gene-nutrient interaction, so finding this mutation in the gene early would help to contain the disease in time.[34] The above example combines personalized nutrition with genetics by linking a single gene in the response to a treatment; however, by integrating each of the omics in personalized nutrition, it would deliver better results (See figure 2).

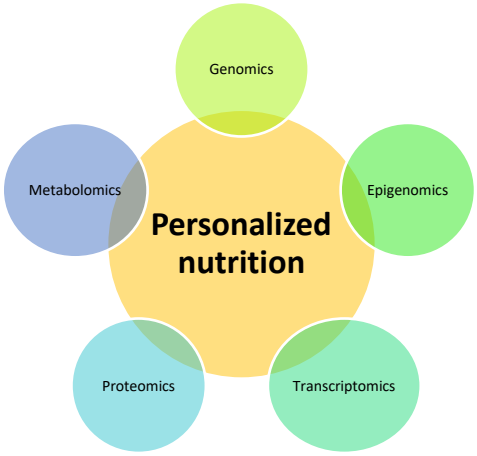

Figure 2. Personalized nutrition with a multiomics approach.[3,6,7]

CONCLUSION

Personalized nutrition applied in different omics have proven to be new tools that help to improve the results of interventions especially in populations with low response to conventional treatments (e.g. patients with metabolic diseases and their comorbidities, phenylketonuria, etc.). However, they present challenges when implemented and interpreted due to the scarcity of health professionals with adequate training adjusted to the various areas of what omics sciences entail, such as the handling of techniques and analysis of results, as well as the correct establishment of which omics are most appropriate for the study of each specific pathology. It is therefore essential to develop personalized nutrition, which will continue to grow in the future.

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