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Nutrigenomics and Gene Modulation Associated with Cardiovascular Diseases

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Abstract. Introduction: Cardiovascular diseases (CVD) are responsible for 31% of global mortality, most in the form of coronary heart disease (CHD) and stroke. Nutrigenomics and nutrigenetics have been tools in the prevention and treatment of cardiovascular diseases. Objective: to review the main polymorphisms related to food metabolism that can be used in the diagnosis and monitoring of cardiovascular diseases. Material and Methods: This study is qualitative and descriptive through a literature review that consulted the PubMed, Virtual Health Library, Scielo, Capes Portal and Google Scholar databases with original articles published in Portuguese and English in the period between January 2010 and September 2021. Results: 26 articles were found as potentially in accordance with the search criteria. After analyzing the abstracts, 17 articles (65.38%) were excluded and 10 (38.46%) articles were selected. Discussion: Benefits of changing the dietary pattern were found that can promote prevention and reduce the risk of cardiovascular events. Conclusion: The use of bioactive substances can contribute positively to modulating the expression of genes associated with increased cardiovascular risk.

Keywords: Nutrigenetics. Cardiovascular. Polymorphisms. Gene Expression. Genomics. Mediterranean Diet.

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Nutrigenômica e a Modulação de Genes Associados a Doenças Cardiovasculares

Resumo. Introdução: As doenças Cardiovasculares (DCV) são responsáveis por 31% da mortalidade mundial, a maioria na forma de doença cardíaca coronariana (DCC) e acidente vascular cerebral. A nutrigenômica e nutrigenética têm sido ferramentas na prevenção e tratamento de doenças cardiovasculares. Objetivo: revisar sobre os principais polimorfismos relacionados ao metabolismo de alimentos que podem ser utilizados no diagnóstico e acompanhamento de doenças cardiovasculares. Material e Métodos: Este estudo é do tipo qualitativo e descritivo através de uma revisão de literatura que foram consultadas as bases de dados PubMed, Biblioteca Virtual em Saúde, Scielo, Portal Capes e Google Acadêmico com artigos originais publicados no idioma português e inglês no período compreendido entre Janeiro de 2010 e Setembro de 2021. Resultados: Foram encontrados 26 artigos como potencialmente de acordo com os critérios de busca. Após a análise dos resumos, 17 artigos (65,38%) foram excluídos e selecionados 10 (38,46%) artigos. Discussão: foram encontrados benefícios da modificação do padrão da dieta alimentar que podem promover a prevenção e reduzir o risco dos eventos cardiovasculares. Conclusão: O uso de substâncias bioativas podem contribuir de forma positiva para modulação da expressão de genes associados ao maior risco cardiovascular.

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Palavras-chave: Nutrigenética. Cardiovascular. Polimorfismos. Expressão Gênica. Genômica. Dieta Mediterrânea.

Nutrigenómica y modulación de genes asociados a enfermidades Cardiovascular

Resumen. Introducción: Las enfermedades cardiovasculares (ECV) son responsables del 31% de mortalidad mundial, la mayoría en forma de enfermedad coronaria (CHD) y accidente vascular cerebral. La nutrigenómica y la nutrigenética han sido herramientas en prevención y tratamiento de enfermedades cardiovasculares. Objetivo: revisar el principales polimorfismos relacionados con el metabolismo de los alimentos que pueden ser utilizado en el diagnóstico y seguimiento de enfermedades cardiovasculares. Material y Métodos: Este estudio es cualitativo y descriptivo a través de una revisión de literatura que fue consultada en PubMed, Biblioteca Virtual em Saúde, Scielo, Portal Capes y Google Scholar con artículos originales publicados en portugués e inglés en el período comprendido entre enero de 2010 y Septiembre 2021. Resultados: Se encontraron 26 artículos como potencialmente según los criterios de búsqueda. Después de analizar los resúmenes, Se excluyeron 17 artículos (65,38%) y se seleccionaron 10 (38,46%). Discusión: se encontraron beneficios al modificar el patrón dietético Alimentos que pueden promover la prevención y reducir el riesgo de eventos cardiovasculares. Conclusión: El uso de sustancias bioactivas puede contribuir a forma positiva para modular la expresión de genes asociados con mayor riesgo cardiovascular.

Palabras clave: Nutrigenética. Cardiovascular. Polimorfismos. La expresion genica. Genómica. Dieta mediterránea.

INTRODUCTION

Cardiovascular Disease (CVD) is a generic term that encompasses a set of associated pathologies, mainly such as coronary heart disease (CHD) (Musunuru; Kathiresan, 2019), cerebrovascular disease, peripheral arterial disease, rheumatic and congenital heart diseases, and venous thromboembolism. Worldwide, CVDs account for 31% of global mortality, most in the form of CHD and stroke (Timmis *et al.*, 2020; Stewart; Manmathan; Wilkinson, 2017).

In Brazil, CVDs have a mortality rate of 31.8% and are considered the leading cause of death. Despite a recent reduction in mortality rates, morbidity from CVDs has had the greatest impact on the cost of hospital admissions in the country (Massa *et al*., 2019; Oliveira *et al*., 2020).

The risk factors associated with the development of CVDs can be modifiable and non-modifiable. Modifiable risk factors are related to: dyslipidemia, obesity, smoking, alcoholism, hyperglycemia, sedentary lifestyle, inadequate diet and use of contraceptive methods; and non-modifiable risk factors are: age, sex, race and positive family history of CVD (Smeltzer *et al*., 2011). However, both can interact, for example, diet can have an influence not on the genome itself, but on the expression of genes related to the development and severity of CVDs.

Nutrigenomics is a new and emerging field of medicine that uses complementary molecular tools, including biochemistry, physiology, proteomics, metabolomics, transcriptomics, and epigenomics, to identify and explain how bioactive compounds in a specific diet can influence gene expression. It is the area that analyzes and reflects on the interaction between nutrients and the genome at the molecular level, to explain how specific nutrients or dietary regimes can affect human health (Gentile *et al*., 2015; Bordoni; Gabbianelli, 2019; Madonna; De Caterina, 2020).

After the completion of the Human Genome Project, nutrigenomics is one of the areas that has expanded, due to greater knowledge of the food metabolism pathway. The human diet contains a complex of biologically active molecules that can act as follows: (a) promoting a direct effect on gene expression, (b) after nutrient metabolism, modulating the activity of transcription factors, and (c) stimulating signal transduction cascades for the induction of transcription factors (Carlberg, 2019; Barabási; Menichetti; Loscalzo, 2020).

In addition, nutrigenomics is the science capable of describing, characterizing, and integrating the interactions between dietary compounds and gene expression throughout the genome (Reddy *et al*., 2018; Carlberg, 2019; Sharma; Dwivedi, 2017). Knowledge about genomic loci related to metabolic and/or regulatory pathways can provide a molecular explanation of how a dietary compound mediates its effects and influences the risk of diet-related diseases (Carlberg, 2019; Gogolev *et al*., 2021).

Considering that nutrigenomics and nutrigenetics have been tools in cardiovascular prevention and treatment, it is important to develop studies that can contribute with reports on the main polymorphisms identified that can support diet personalization and optimize CVD prevention. The objective of the present study is to review the main polymorphisms related to food metabolism that can be used in the diagnosis and monitoring of cardiovascular diseases.

METHODOLOGY

This is a qualitative and descriptive study through a literature review prepared with the analysis of scientific publications that associated nutrigenomics and nutrigenetics with cardiovascular diseases.

The databases used were: PubMed, Virtual Health Library, Scielo, Capes Portal and Google Scholar, involving all original articles published in Portuguese and English between January 2010 and September 2021. The search strategy used was the use of the following descriptors: “Genes”, “Cardiovascular Diseases”, “polymorphism”, “nutrigenomic”, “nutrigenetic”, “doenças cardiovasculares”, “polimorfismos”, “nutrigenômica” and “nutrigenetica”.

The articles were analyzed to identify studies that met the review criteria. The inclusion criteria were: original articles such as randomized clinical trials and clinical trials presenting the full text,

eligibility criteria, adequate description of the nutritional intervention and/or genomic analysis methods, study design with identification of the main polymorphisms associated with nutrigenomics, nutrigenetics and cardiovascular diseases.

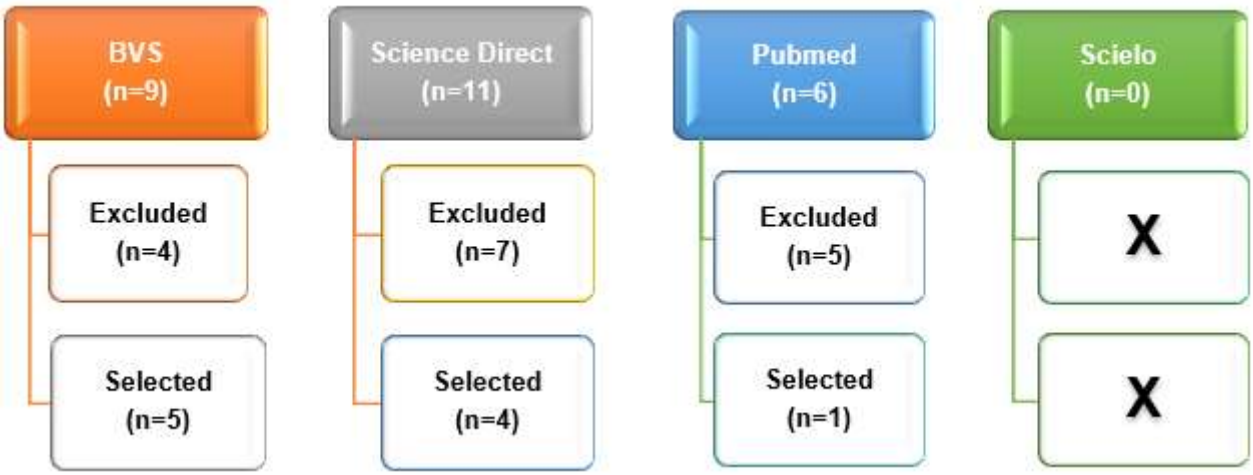
After this search strategy, the association with the terms was redefined. Literature review studies and duplicate articles were excluded. In addition, studies that did not have defined eligibility criteria or did not have a design on the relationship between identification of polymorphisms associated with cardiovascular diseases.

RESULT AND DISCUSSION

Twenty-six potential articles were found according to the search criteria and association of descriptors. After analyzing the abstracts, 17 articles (65.38%) were excluded for the following reasons: they did not present in the abstract any association of the topic with nutrigenomics or cardiovascular disease, or they did not have a correlation with polymorphisms in cardiovascular disease. In addition, duplicate articles and articles on systematic reviews or bibliographic reviews were excluded.

In Figure 1 shows the organization of the selection of articles for the present study, in which 10 (38.46%) complete articles were selected for analysis.

Figure 1. Study Selection Diagram of Databases



Source: Prepared by the authors (2024)

Foods With the Potential to Modulate Genes Related to Cardiovascular Diseases

The selected studies found benefits from changing the dietary pattern that can promote prevention and reduce the risk of cardiovascular events. These effects can be explained and unraveled by the

insertion of nutrigenomic analysis to identify the main polymorphisms and genes associated with cardiovascular disease, in addition to understanding the interaction between the gene and the nutrient.

The articles reviewed showed that the use of bioactive compounds such as curcurmin and extra virgin olive oil (EVOO) have the potential to increase the expression of certain genes and reduce cardiovascular risk. The nutritional properties of these compounds can contribute to improving the lipid profile, glycemic profile and reducing inflammatory markers at the cellular level, and one of the main mechanisms is related to the modulation of gene expression.

A randomized, double-blind, crossover study by Martín-Peláez *et al*. (2015), in humans with 18 healthy individuals, evaluated the intake of 25 mL/day of olive oil to investigate the effects of EVOO intake and its phenolic contents on the expression of genes associated with changes in blood pressure and involved in the Angiotensin Converting Enzyme (ECA) system. They found that daily consumption of EVOO rich in phenolic compounds was effective in modulating the expression of genes related to the ACE system, leading to a reduction in systolic blood pressure.

In addition, Bordoni *et al*. (2019) found beneficial results with the use of EVOO and Nigella sativa (NG), as they induced antioxidant and epigenetic mechanisms that would be important in the prevention and control of inflammatory processes in diseases such as diabetes, obesity, and cardiovascular diseases. The model used was performed in cell cultures to investigate the properties of two high-quality oils, EVOO and NG, in an in vitro model of low-grade inflammation of human macrophages (THP-1 cells). NS oil had a more efficient response in controlling pro-inflammatory cytokines, and on the other hand, EVOO enhanced the neutralization process and improved redox imbalance. In addition, no cytotoxic effects were observed and a protective effect on cell membrane fluidity.

Abdolahi *et al.* (2019) evaluated 74 patients with migraine, which is a neuroinflammatory disease, through a clinical trial over a period of 2 months, allocated into four groups with different interventions: ω-3 fatty acids, nanocurcumin group, combination of the two bioactives, or placebo group. The results showed better responses in the group that received the combination of ω-3 fatty acids and nano-curcumin in the neuroinflammatory state in patients with migraine regarding the reduction of levels and changes in the expression of COX-2/iNOS mRNA genes, and therefore reduced the neuroinflammatory effects.

In the study that Shafabakhsh *et al*. (2020) carried out a double-blind and controlled clinical trial that involved 60 patients with diabetes and cardiovascular diseases; in the intervention group they ingested 1000mg/day of curcumin for 12 weeks, which had beneficial effects on the Pittsburgh Sleep Quality Index, increased antioxidant capacity (TAC), increased glutathione levels, reduced malondialdehyde (MDA) and upregulation of peroxisome proliferator-activated receptor gamma

(PPAR-γ). Curcumin supplementation promoted beneficial effects in reducing inflammatory factors, reducing oxidative status and modulating PPAR-γ gene expression.

Several studies suggest that the Mediterranean Diet (Med Diet) is considered one of the most effective in the treatment of cardiovascular diseases, and its use is widespread and publicized in studies in Cardiology. In general, it consists of guidelines that recommend high intake of extra virgin olive oil (cold pressed), vegetables, including green leafy vegetables, fruits, cereals, nuts and legumes, moderate intake of fish and other meats, dairy products and red wine, and low intake of eggs and sweets (Davis *et al*., 2015), reinforcing the importance of using nutrigenomics in the treatment of diseases.

According to the results of the studies found, the Med Diet contributed to the prevention or reduction of disease damage in carriers of polymorphisms related to cardiovascular disease, in which the inflammatory process and oxidative stress stand out San-Cristobal *et al*., (2017). In board 1, presents the selected studies that addressed Nutrigenomics with Cardiovascular Diseases.

Board 1: Estudos que associaram a Nutrigenômica e a Doença Cardiovascular

Author	Objective	Genes/Polymorphism	Subjects	Intervention	Resultados
Barber-Chamoux *et al.*,(2018)	To evaluate the vascular effect of acute curcumin intake and its nutrigenomic impact on circulating immune cells	Genes involved in the regulation of different cellular functions, such as chemotaxis (CXCR7, CCR7 or CX3CR1), cell adhesion (ITGA5, ITGB2, CD40 or PECAM1) or cholesterol efflux (ABCA2, ABCC2 or ABCB4)	Randomized, double-blind, crossover study, 18 healthy smokers	The groups consumed either placebo treatment or 5 g curcumin. Before and 2 h after ingestion, vascular function measurements were performed using flow-mediated dilation (FMD). In addition, endothelial function in the microcirculation and blood pressure were assessed.	Curcumin intake may be of better interest for preventing endothelial dysfunction rather than restoring more established dysfunction, suggesting that curcumin may be a nutraceutical of special interest for maintaining endothelial function.
Božina *et al*., (2018)	To examine the interaction between dietary patterns and AT1R polymorphism in relation to the risk of metabolic syndrome (MetS) and its implication with cardiovascular risk.	The association between the 1166A > C polymorphism of the Angiotensin II type 1 receptor (AT1R) gene and the presence of MS and cardiovascular risk.	528 Croatian participants (343 women, 185 men) were allocated into two groups: 265 patients with MetS and 263 controls (without MetS criteria).	Each participant was assessed on their diet type (Mediterranean, continental and mixed diet). Genomic DNA was extracted from leukocytes using the salting out procedure and genotyping of AT1R 1166A>C	Diet choice may undermine the potential genetic risk of the AT1R 1166A>C polymorphism, and people who are variant carriers may spontaneously choose the Mediterranean Diet.
D'amore *et al.*, (2016)	To identifying genes and miRNA expression changes mediated by expression patterns of acute extra virgin olive oil (EVOO) intake in PBMCs in multiple sclerosis	A total of 8708 genes were evaluated to identify those associated with the intake of EVOO with high polyphenol content by comparing gene expression in PBMCs.	12 healthy individuals (mean age 29 ± 2 years) and 12 patients at first diagnosis of MS (35 ± 3 years) were recruited for this study.	Prior to both dietary interventions (high polyphenol and low polyphenol (EVOO) intake), patients followed a 1-week washout period in which no olive oil consumption was allowed.	EVOO intake induces different effects also at the miRNome level, including the promotion of miRNAs with anti-inflammatory action
De Lorenzo *et al*., (2017)	To investigate the postprandial plasma ox-LDL level and the expression of 13 genes related to oxidative stress and inflammation after the tocopherol-rich Mediterranean meal (TEM) and the high-fat Western meal (HFM).	Inflammatory genes: BCL2, (NM_633); ASP1(NM_33292); CASP8(NM_1228); IL12A(NM_1569);TNF-α(NM_594).Oxidative stress genes LOX12(NM_697)CCL5(NM_2985); DUOX2 (NM_14080);GCLC, PX1, PRDX, UCP2 (NM_3355).	25 healthy participants, within a program of the Section of Clinical Nutrition and Nutrigenomics of the University of Rome 'Tor Vergata'.	TEM consisted of a menu with a total of 1318.68 kcal (41.37% from carbohydrates; 16.53% from proteins; 42.10% from total fat). HFM consisted of a total of 1144.17 kcal (26.84% of total kcal from carbohydrates; 18.18% of total kcal from protein; 54.98% of total kcal from total fat).	There was a positive effect of TEM, therefore regular consumption of the Mediterranean diet may be essential to reduce daily events depending on postprandial inflammation and oxidative stress, related to the outbreak of CVD.
De Luis *et al*., (2017)	To evaluate the relationship between weight loss and changes in adipokine levels after two hypocaloric diets in obese individuals with rs16147 polymorphism of	Neuropeptide Y Gene rs16147 Polymorphism	A sample of 283 non-diabetic obese outpatients was prospectively enrolled. The inclusion criterion was a body mass index (BMI) ≥ 30.	Patients were randomly allocated to one of two diets for a period of 3 months. Diet I was low in carbohydrate and provided 1507 kcal/day (38% carbohydrate, 26% protein, 36% fat). Diet II was low in	The rs16147 genotype affected the reduction of insulin resistance and insulin levels in response to two different hypocaloric diets in obese individuals, with a lack of

	the neuropeptide Y gene with cardiovascular risk factors			fat and provided 1500 kcal/day (53% carbohydrate, 20% protein, 27% fat).	response in individuals with the major allele.
Fallaize *et al*. (2016)	To investigate interactions between APOE genotype and habitual dietary fat intake and modulations of fat intake on metabolic outcomes; To determine whether gene-based Personalized Diet results in greater dietary change than standard dietary advice and non-gene-based Personalized Diet; and To assess the impact of APOE risk knowledge on cardiovascular disease	Polymorphism in the APOE gene (rs429358 and rs7412). The e4 allele is most associated with increased total and LDL cholesterol. A genetic variation a genetic variation that can be modified by diet, i.e. E3 / E4 or E4 / E4 (E4+)] or "no risk" [E2 / E2, E2 / E3, E3 / E3 (E42)]	A total of 1466 of the 1607 participants randomly assigned to the Food4Me study were genotyped for APOE and included in the baseline analysis.	In the Food4Me study the following were allocated: -Level 0 (L0): (control group): non-personalized dietary advice from the European healthy eating guide. Level 1 (L1): personalized dietary advice based on individual food intake data alone. -Level 2 (L2): personalized dietary advice based on individual food intake and phenotypic data. -Level 3 (L3): personalized dietary advice based on individual food intake, phenotypic and genotypic data.	APOE status was associated with baseline TC, with higher concentrations in E4+ participants. Personalized nutrition (PN) was more effective in reducing saturated fat (SFA) intake.
Perrone *et al.*, (2019)	To examine the metabolic profile, glycemic, lipid profiles and oxidative status (MDA, oxLDL-C); and the evaluation of gene expression of genes belonging to the lipid, inflammatory and oxidative stress pathway	Genes related to oxidative stress, MIF, SOD1, CAT, CCL2, NFkB and cardiovascular risk, such as ACE, USF1 and APOE	22 healthy volunteers were recruited at the Division of Clinical Nutrition and Nutrigenomics of the University of Rome Tor Vergata	The intervention group received 25 g of p-EVOO, and the control group received 25 g of C-OO containing 9.4 and 2.3 mg of hydroxyphenylethanol and derivatives in 20 g of oil, respectively.	Significant upregulation of SOD1, CAT and USF1 was found. Consumption of 25 g of p-EVOO reduces oxidative stress, protection of LDL-C particles, reduction of cardiovascular risk.
Rizzi *et al.*, (2016)	To examine whether the interaction between polyphenol and anthocyanin intake and PON1 genetic variants can modulate cardiovascular health biomarkers in a healthy Italian population.	Paraoxonase 1 (PON1) polymorphism and/or the level of PON1 expression. PON1, PON2, and PON3 are a family of genes clustered together on the long arm of human chromosome 7 (q21.22)	Observational Nutrigenetic Study on 500 volunteers (age range 20 to 85 years), as defined in the ATHENA Project.	Dietary assessment was performed by 24-h dietary recalls. 24-h recall data were recorded at least three times per year, once during the first clinical visit and then every 3–4 months. For data collection and dietary nutrient composition estimation we used the Diet Monitoring Solution (DMS).	The role of PON1 as a susceptibility gene for cardiovascular health under high antioxidant intake. Protective genotypes were identified in 4 independent polymorphisms, showing an association with increased HDL levels.
	To explore associations and potential interactions between MedDiet adherence and genetic background across the	SNPs: rs6323 for MAOA, rs5082 for APOA2, rs708272 for CETP, ADRB2 (rs1042713 and rs1042714); AGT (rs5051 and rs699); APOE (rs429358 and	A total of 1263 volunteers participated, providing complete data on anthropometric measurements and	They were allocated to the control group, or to 3 different levels of intervention. General information about healthy eating was provided to participants included in the control	The results of the present study showed that initial adherence to the MedDiet is associated with beneficial effects on anthropometric measures and

San-Cristobal *et al*., (2017)	Food4Me web-based nutritional intervention.	rs7412); FTO (rs1121980 and 9939609); GC (rs2282679, rs7041, and rs4588); and CETP (rs3764261 and 708272, VDR(rs1544410 and rs2228570, rs1042714, rs699, rs7412, rs9939609, rs2282679 and rs3764261.	providing adequate samples for biochemical and genetic analyses.	group, while personalized nutritional advice was provided to participants included in the 3 personalized nutritional advice groups, feedback was received based on diet alone, diet and phenotype, or diet phenotype and genotype.	may overcome an adverse genetic load.
Schüler *et al.*, (2017)	To examine the effects of a high saturated fat (HF) diet on ACE within the NUtrigenomics in Twins Study (NUGAT) Analysis.	Frequent insertion/deletion (I/D) polymorphism located in the 16th intron of the ACE gene (Alu I/D).	A total of 46 pairs of healthy, non-obese twins, 34 monozygotic and 12 dizygotic, aged 18 to 70 years and body mass index (BMI) 18 to 29 kg/m2.	Subjects underwent a 6-week isocaloric dietary intervention with a high-carbohydrate, low-fat diet (LF: 55% carbohydrate, 30% fat, 15% protein). All subjects were required to complete 5 dietary records over the 12-week dietary intervention period.	HF diet-induced increase in serum ACE concentrations reveals that ACE is a potential molecular link between dietary fat intake and hypertension and cardiovascular disease (CVD).

Source: Prepared by the authors

Roncero-Ramos *et al*. (2018) sought to evaluate the effects of consuming two diets over a 36-month period, the Mediterranean diet and the low-fat diet, on glucose homeostasis in patients with coronary heart disease in the CORDIOPREV study. According to the genetic variant of the NLRP3 inflammasome, the group that followed the Med Diet had better results regarding the control of glucose homeostasis and was dependent on the genetic variation in the inflammasome. Therefore, the increase in the insulin sensitivity index (ISI) in AG+AA carriers for the rs10733113 SNP polymorphism and CT+TT carriers for the rs4612666 SNP polymorphism after consumption of the Med Diet (Roncero-Ramos *et al*., 2018).

Accordingly, inadequate intake of lipids and carbohydrates in high-fat and/or high-glycemic diets can promote an imbalance in the regulation of gene expression, contributing to the development of obesity, diabetes, and metabolic syndrome, increasing cardiovascular risk (Bravo-Ruiz *et al*., 2021).

In support of these findings, the study by Ortega-Azorín *et al*. (2012) sought to analyze the associations of the Fat Mass and Obesity (FTO) and Melanocortin-4 Receptor (MC4R) genes with adherence to the Mediterranean Diet. A total of 7,052 individuals at high cardiovascular risk participated, and it was observed that high adherence to the Mediterranean diet was able to neutralize the negative factors of the genetic predisposition of the FTO-rs993960 and MC4R-rs17782313 polymorphisms in relation to type 2 diabetes, related to increased cardiovascular risk.

The basis of diets includes the consumption of lipids and carbohydrates, which can promote the regulation of gene expression through molecules that detect these macronutrients and act as transcription factors. An example is the peroxisome proliferator-activated receptor (PPAR), which is activated by some fatty acids or their derivatives, and the carbohydrate response element and binding protein (ChREBP), activated by glucose-derived metabolites, which plays a fundamental role in homeostasis metabolism, mainly in glucose and lipid metabolism (Bravo-Ruiz *et al*., 2021).

Personalized dietary advice, when based on individual needs and considering the genetic profile, is considered one of the most effective strategies for the prevention and treatment of diseases associated with obesity, and especially cardiovascular disease. This personalized advice is established with nutrigenetics considered as precision nutrition, as it considers specific genetics and the factors that can explain interindividual variability in the response to the individual eating pattern (Barrea *et al.*, 2020).

Perspectives on Nutrigenomics and Nutrigenetics

There is great complexity in studies involving nutrigenomics, whether in the knowledge of nutrient-induced changes on the transcriptome (the complete set of transcripts, such as messenger RNAs, ribosomal RNAs, transport RNAs and microRNAs), proteome (the total sum of all proteins) and/or

metabolome (the sum of all metabolites), since there is variability between individuals and/or environmental conditions. Nutrigenetics studies the effect of genetic dispositions: mutations, SNPs (single nucleotide polymorphism), copy number variation and epigenetic alterations on the biology of nutrition. Epigenetics contributes to the description of heritable changes caused by mechanisms other than alterations in the DNA sequence (Sharma; Dwivedi, 2017; Reddy *et al*., 2018).

Emerging technologies in the field of epigenetics are seeking to unravel the molecular mechanisms of how genetic information other than DNA sequence can affect gene function, particularly the impact of diet and environment on genomic, transcriptional, and developmental regulation, including DNA methylation, acetylation, histone modification paramutations, and gene silencing (Reddy *et al*., 2018; Ahn *et al*., 2021).

Some of the leading next-generation sequencing (NGS) technologies, such as RNA sequencing, chromatin immunoprecipitation followed by sequencing (ChIP-seq), and formaldehyde-assisted identification of regulatory elements followed by sequencing (FAIRE-seq), enable the unbiased assessment of genome-wide mRNA expression, transcription factor binding, histone modifications, and chromatin nutrients (Meyer; Liu, 2014; Gogolev *et al*., 2021). These tests are useful in the application of nutrigenomics, whether in research or for conducting panels in clinical practice.

There are prospects for the integration of research networks through large global research consortia in this field, such as the ENCODE and Roadmap Epigenomics projects, which have collected large amounts of data on the basal state of more than one hundred human cell lines, primary human tissues, and cell types. In addition, the trend in this study is recent longitudinal molecular assessments of individuals in relation to their lifestyle decisions, such as the Personalized Omics Profiling Project and the Pioneer 100 Wellness Project, which have contributed data on the identification of polymorphisms for nutrigenomics (Carlberg, 2019).

There are expectations that nutrigenomics will be associated with the use of integrated platforms, such as the ENCODE and Roadmap Epigenomics projects, for example (CARLBERG, 2019). According to the outlook, there will be the integration of these data sets, together with modern bioinformatics tools that should revolutionize more quickly the understanding of the interaction of nutrition with health and disease (Reddy *et al*., 2018).

CONCLUSION

The influence of Nutrigenomics on diet and cardiovascular diseases is a strategy that can enhance the effectiveness of diet prescriptions, and it was possible to identify different types of modulation of bioactive nutrients to reduce inflammation and oxidative stress, which are important factors in the

progression of cardiovascular diseases. In addition, more studies are needed to identify new genetic markers related to dietary patterns that are associated with the progression of cardiovascular disease and with beneficial effects to promote disease control. The trend in clinical practice and nutritional counseling for more promising results is the addition of nutrigenomics for personalized treatment of the population to meet individual demands, since genetic variability is essential to understand the different responses to dietary treatment. According to the survey, nutrigenomics showed positive impacts between dietary patterns and the prevention of cardiovascular disease. Among the main dietary interventions, the Med Diet is more effective in treating cardiovascular diseases, since most foods, such as EVOO, contain bioactive compounds that have positive effects on nutrigenomic findings. Therefore, the analysis of polymorphisms and genes associated with cardiovascular disease may undergo changes and modifications according to the type of dietary pattern of the population. The use of bioactive substances may contribute positively to modulating the expression of genes associated with increased cardiovascular risk.

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