J Lipid Atheroscler. 2026 Jan;15(1):26-47
https://doi.org/10.12997/jla.2026.15.1.26
pISSN 2287-2892·eISSN 2288-2561

JLA Journal of Lipid and Atherosclerosis

Review

Check for updates

Selected Genes Associated With CVD-Related Diseases, Pathways, and Nutrigenetics

Seyma Sehadet Tasdemir [1,2] **Gamze Akbulut** [3]

[1]Department of Nutrition and Dietetics, Bitlis Eren University, Bitlis, Turkey
[2]Department of Nutrition and Dietetics, Gazi University, Ankara, Turkey
[3]Department of Nutrition and Dietetics, Kent University, Istanbul, Turkey

OPEN ACCESS

Received: Mar 15, 2024
Revised: Jul 3, 2024
Accepted: Jul 24, 2024
Published online: Sep 17, 2025

Correspondence to
Seyma Sehadet Tasdemir
Department of Nutrition and Dietetics, Bitlis Eren University, Rahva Campus, Beş Minare District, Ahmet Eren Boulevard, 13100 Bitlis, Turkey.
Email: sehadettasdemir@gmail.com

ORCID iDs
Seyma Sehadet Tasdemir
https://orcid.org/0000-0002-5151-1658
Gamze Akbulut
https://orcid.org/0000-0003-0197-1573

Funding
None.

Conflict of Interest
The authors have no conflicts of interest to declare.

Data Availability Statement
Data sharing is not applicable to this article because no datasets were generated or analyzed in the current study.

ABSTRACT

Any dysfunction or obstruction in blood circulation can lead to the development of cardiovascular disease (CVD), which is multifactorial but primarily caused by atherosclerosis. Nutrition is considered as the most significant modifiable environmental factor, with a direct influence on cardiovascular risk mediated by triggering inflammation, oxidative stress, and various physiological, molecular, and biological changes. Despite these well-established mechanisms, targeting nutrition has not led to the expected reduction in CVD mortality rates. This discrepancy is thought to be due to interindividual variability in genetic factors that modulate responses to nutritional interventions. Genetic variants can interact with specific nutrients and dietary components, influencing their effects on cardiovascular health. Advances in nutrigenetics and nutrigenomics which explore nutrient-gene interactions, have led to the development of the concept of personalized nutrition. This approach aims to prevent CVD and other diseases by tailoring dietary treatments to individual genotypes identified through genetic polymorphisms. It is suggested that life expectancy and sustainable healthy living can be enhanced by aligning dietary treatments with specific genetic profiles associated with CVD. Therefore, this review discusses genes linked to CVD and explores how gene-driven differences in dietary responses affect cardiovascular health outcomes.

Keywords: Single nucleotide polymorphism; Nutrigenetics; Nutrigenomics; Cardiovascular diseases; Diet

INTRODUCTION

Blood circulation plays a crucial role in transporting nutrients and oxygen to tissues and organs, while also removing metabolic wastes from the body, through the cardiovascular system.[1] Any dysfunction or obstruction in blood circulation can lead to the development of cardiovascular disease (CVD), which is multifactorial but primarily caused by atherosclerosis.[2,3] CVD encompasses a range of circulatory disorders including coronary artery diseases, cerebrovascular accidents, dyslipidemia, hypertension, heart failure, atherosclerosis, congenital heart diseases, and vascular diseases.[4-7] According to a report by the World Health Organization (WHO), CVD is the leading cause of death globally.

Author Contributions

Resources: Tasdemir SS; Software: Tasdemir SS; Validation: Akbulut G; Visualization: Tasdemir SS; Writing - original draft: Tasdemir SS, Akbulut G; Writing - review & editing: Akbulut G.

In 2019, approximately 17.9 million people died from CVD, accounting for 32% of all deaths worldwide. Notably, 85% of these deaths were due to stroke and heart attack.[8]

The most significant behavioral risk factors for CVD include lack of physical activity, alcohol and tobacco use, and an inadequate and unbalanced diet. These factors contribute to increased blood sugar, blood pressure, and blood lipids, as well as to overweight and obesity.[8,9] Nutrition, which directly influences cardiovascular risk through the initiation of inflammation, oxidative stress, and various physiological, molecular, and biological changes, is recognized as the most critical modifiable environmental risk factor.[10-13] It also indirectly contributes to the development of CVD by affecting the lipid profile, blood pressure, body mass, and the risk of diabetes and atherosclerosis.[10] Therefore, nutritional recommendations have become a global priority for reducing the risk of CVD, leading to the publication of various guidelines.[14-18] These guidelines are designed for populations rather than for individuals or specific groups.[19] Despite these efforts, the reduction in CVD mortality rates has not reached the expected levels. The differing impacts of genetic factors on responses to nutritional interventions are believed to be a contributing factor to this discrepancy.[20] Variations in genetic profiles among individuals and specific ethnic groups affect nutrient requirements, metabolism, and responses to nutritional and dietary interventions. It has been suggested that tailored dietary advice for individuals with specific genotypes may be more effective than general dietary guidelines in preventing chronic diseases.[19]

Precision nutrition operates on the principle that a single diet does not suit everyone, recognizing that individuals have unique responses to nutrients. This approach considers how genes react to nutrients, as well as how nutrients interact with epigenetic markers and other regulatory mechanisms that influence genome stability, metabolome, proteome, gut microbiome, and gene expression.[21] For example, the effects of the apolipoprotein E (*APOE)* gene and the methylenetetrahydrofolate reductase (*MTHFR)* gene on cholesterol metabolism and folate metabolism, respectively, are well documented.[22,23] Consistent cardiovascular effects of interactions between genes such as angiotensin-converting enzyme (*ACE),* fat mass and obesity-associated *(FTO),* transcription factor 7-like 2 *(TCF7L2),* melanocortin 4 receptor *(MC4R),* brain-derived neurotrophic factor *(BDNF),* peroxisome proliferator-activated receptor *(PPAR),* apolipoprotein A *(APOA)*, and fatty acid desaturase (*FADS)* and macronutrients have been demonstrated in the general population.[24] In a study with obese and overweight individuals, a nutrigenetic dietary intervention reduced blood lipid levels and was reported to be a promising intervention for cardiometabolic diseases.[25] A systematic review highlighted the critical need to develop nutrigenetic interventions, pointing out the direct effects of macronutrient intake, monounsaturated and polyunsaturated fatty acids, as well as dietary supplements and nutraceuticals on blood lipid levels.[26] For example, studies have shown that variations in the *APOE* gene and interactions with dietary fat, saturated fatty acid, and carbohydrate intake are associated with dyslipidemia.[27] Additionally, dietary patterns characterized by frequent consumption of soybeans, mushrooms, dairy products, and nuts, accompanied by low meat intake, have been associated with reduced CVD complications through interactions with the adiponectin (*ADIPOQ*) and MTHFR genes.[28] Furthermore, a diet high in beans and legumes like soybeans and low in fats, junk food, and sweets has shown interactions with the 9p21 polymorphism.[29] Other studies have also demonstrated that gene polymorphisms associated with CVD risk can interact with diet.[30-32] A flowchart of the relationship between CVD and personalized nutrition is shown in **Fig. 1.** These genetic variants may determine individual responses to specific nutrients and dietary components, ultimately affecting cardiovascular health. Therefore, this review explores nutrigenetic effects on CVD.

JLA Journal of Lipid and Atherosclerosis

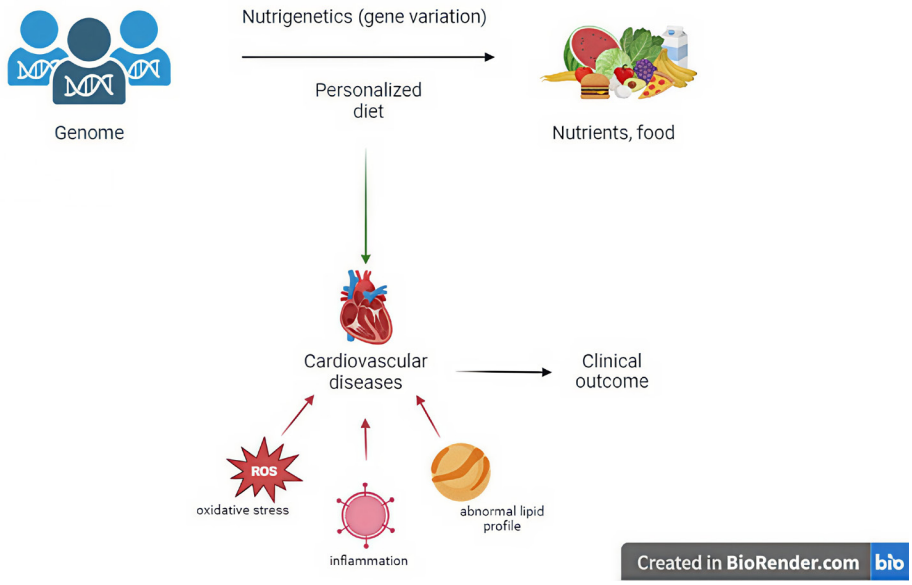

Fig. 1. Relationship between cardiovascular diseases and personalized nutrition.

CARDIOVASCULAR DISEASES, NUTRIGENETICS, AND NUTRIGENOMICS

The field of nutrition genomics, or molecular nutrition, has developed from research in genetics and nutrition, significantly influenced by the Human Genome Project (HGP).[12,33] This discipline explains how food intake interacts with the human genome, aiding in understanding gene expression and metabolic responses that influence individual susceptibility to diseases.[34] Nutrition genomics encompasses the areas of nutrigenomics and nutrigenetics, which, despite their relatedness, differ fundamentally.[35] Nutrigenomics is defined as a research field that explores the molecular relationships between genes and nutrients in disease prevention or treatment by altering gene expression and metabolic responses through dietary components.[34,36,37] It aims to uncover the connections between nutrients, the human genome, and health, incorporating fields such as transcriptomics, epigenomics, metabolomics, and proteomics.[36] Conversely, nutrigenetics focuses on how genetic variations, such as single nucleotide polymorphisms (SNPs), affect dietary responses.[33,38,39] The relationship between nutrigenetics, nutrigenomics, and CVD is presented in **Fig. 2**.

It has been stated that these genetic variations, which are key to human growth and development, interact with the environment and may affect the risk of CVD through altering the responses to dietary intake.[12,40] Consequently, advancements in nutrigenetics and nutrigenomics, which explore the interactions between food and genes, have led to the development of the concept of personalized nutrition (PN). This approach aims to prevent the onset of diseases such as CVD and to mitigate associated risks.[20,33] It has also been posited that determining genetic polymorphisms related to CVD and applying genotype-based dietary treatments can lengthen life expectancy and promote a sustainable healthy lifestyle.[12] However, a recent systematic review of 266 gene-diet interactions, including variants in cholesterol ester transfer protein (*CETP*) and alcohol dehydrogenase 1C (*ADH1C*), found that only 18.8% had a significant association with CVD. The heterogeneity

https://doi.org/10.12997/jla.2026.15.1.26

JLA Journal of Lipid and Atherosclerosis

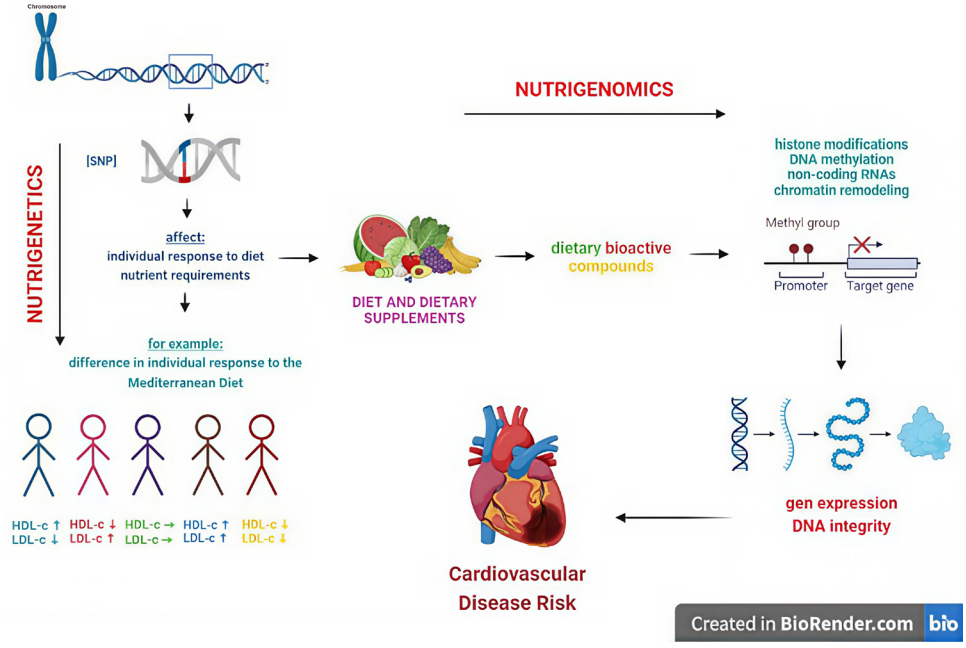

Fig. 2. Relationship between nutrigenetics, nutrigenomics, and cardiovascular disease.
SNP, single nucleotide polymorphism; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

of the studies posed limitations on the analytical measures. Additionally, it has been highlighted that dietary components may also regulate genes or DNA, potentially impacting CVD risks.[41] Meanwhile, another extensive study examining the effects of saturated fatty acids (SFAs) and monounsaturated fatty acids (MUFAs) on CVDs emphasized the need to integrate microbiomic, epigenomic, genomic, and metabolomic data with dietary responses into personalized nutrition strategies.[42]

GENETICS OF CARDIOVASCULAR DISEASES

Studies have focused on the analysis of gene-related molecules to understand disease mechanisms. While these molecules may not directly cause diseases, they can serve as markers that improve the understanding of a patient's prognosis and risk. Alterations in gene expression levels can signal the presence of a disease state, thus potentially serving as biomarkers.[43]

1. Candidate gene approaches

The candidate gene approach is a basic research method based on the hypothesis that a specific gene plays a role in a certain phenotype or clinical effect. This method is one of the first and simplest approaches to understanding the molecular and cellular functions of genes.[44] For example, a candidate gene study has shown that the *ACE* insertion/deletion (I/D) polymorphism is a strong risk factor for coronary heart disease.[45] In these studies, challenges such as inadequate sample sizes, poor population homogeneity, and uncertainties about whether the proteins encoded by the selected genes are mechanistically related can lead to erroneous results.[46] Nevertheless, research on genetic biomarkers has successfully pinpointed critical single genes or variants by concentrating on candidate genes in

https://doi.org/10.12997/jla.2026.15.1.26

monogenic heart disorders. Notably, the *APOE*, *APOA5*, and *MC4R* genes have been identified as key determinants of plasma cholesterol levels, plasma triglycerides, and body weight.[47]

2. Genome-wide association studies (GWAS)

The completion of the Human Genome Project paved the way for the initiation of GWAS, which continue to be conducted.[48] The genetic variants most commonly studied in GWAS are SNPs, which account for 80% of genetic variation between individuals, but copy number variations and sequence variations are also studied.[49,50] A polymorphism is defined as genetic variations with a frequency of 1% or higher. It represents a change in a single nucleotide in the DNA sequence.[51] SNPs are known as the most common form of genetic variation,[52] and It is estimated that there are about 10 million SNPs in the human genome.[53]

In GWAS, the 9p21.3 SNPs were the first identified loci associated with CVD.[54] Approximately 75% of the global population carries this risk allele, which has been shown to contribute to coronary atherosclerosis.[55] The chromosome 9p21 locus is considered highly significant as it represents the genetic variant with the greatest risk.[56] Subsequently, loci for the long non-coding regulatory RNA *ANRIL* (antisense noncoding RNA in the INK4 locus) were identified in gene-free regions, and these loci have been linked to an increased risk of myocardial infarction. Another gene identified through GWAS is sortilin, also known as *CELSR2*/*PSRC1*/*SORT1*. While the exact mechanism of variations in this gene remains unclear, it is known to influence cholesterol metabolism. *FTO*, a gene significantly associated with obesity and diabetes, was later found to also be associated with the risk of myocardial infarction.[47] Familial hypercholesterolemia is characterized by monogenic mutations in the genes encoding *APOB*, proprotein convertase subtilisin/kexin type 9 (*PCSK9*), and low-density lipoprotein receptor (*LDLR*). Loss-of-function variants in these genes cause increased blood cholesterol levels and a four-fold higher risk of CVD.[55] More than 200 loci have been reported to be related to CVD and myocardial infarction since 2007.[57] In addition, the importance of CVD for aging and death has been emphasized in GWAS. For example, the *APOE* locus, which is associated with both dementia and coronary artery disease, has been strongly associated with longevity.[58] The identification of genetic risk factors for numerous diseases through GWAS has been pivotal in the field of human genetics.[59]

3. Polygenic risk score

It has been stated that individually defined polymorphisms may be insufficient to predict disease risk. Consequently, polygenic risk scores (PRSs) have been developed through GWAS to predict disease risk by summing the number of risk variant alleles in the human genome.[55,60] A PRS, also known as a genetic risk score, can be calculated in 2 ways: the unweighted genetic risk score, which sums the number of risk alleles regardless of each allele's effect size, and the weighted genetic risk score, which aggregates alleles taking into account the actual effect of each SNP on the risk factor.[47] In one study, genetic risk scores constructed from 13 genetic variants associated with myocardial infarction or coronary heart disease were found to be independent predictors of cardiovascular events and elevated coronary artery calcium.[61] Inouye and colleagues[62] calculated a genomic risk score using lifelong germline DNA to classify individuals in general populations in terms of coronary artery disease (CAD) risk, demonstrating the importance of using genomic information. PRSs have been created to predict the genetic risk of CVDs, type 2 diabetes, and dyslipidemia. It was shown that a healthy lifestyle reduces the incidence of disease in groups with high PRSs.[63] It was also emphasized that the development of artificial intelligence-based PRSs could increase the accuracy of risk predictions.[64]

https://doi.org/10.12997/jla.2026.15.1.26

JLA Journal of Lipid and Atherosclerosis

GENES ASSOCIATED WITH CARDIOVASCULAR DISEASES

In total, 321 chromosomal loci have been identified that map to coronary artery disease risk and the pathophysiological pathways of atherosclerosis, including blood pressure, lipid metabolism, immune response and inflammation, nitric oxide (NO) signaling, thrombosis, vascular remodeling, proliferation and transcriptional regulation, pathways associated with ncRNAs, adiposity, and insulin resistance.[65] Most of the identified loci are in genes associated with lipid metabolism and inflammation.[13,20]

1. *APOE* gene

APOE, a 34 kDa protein consisting of 299 amino acids, is a key component of triglyceride-rich lipoproteins. It is present on the surface of very low-density lipoprotein (VLDL), intermediate-density lipoprotein (IDL), high-density lipoprotein (HDL), and chylomicrons.[66] Therefore, its role in lipid metabolism and cholesterol absorption is well known. The *APOE* gene has three main alleles: ε2, ε3, and ε4.[67] The ε3 (rs7412-C, rs429358-T) allele is the most common. The ε4 (rs7412-C, rs429358-T) allele is associated with higher plasma APOB and low-density lipoprotein cholesterol (LDL-C) concentrations, with a greater susceptibility to CVD.[68] In addition, individuals with the *APOE*ε4 allele were reported to be more sensitive to dietary modifications than individuals with the *APOE* ε3 or ε2 alleles.[67,69]

2. *APOA1* gene

APOA1, which consists of 243 amino acids,[70] is synthesized in the liver and intestine and serves as the primary apolipoprotein component of HDL, playing a significant role in reverse cholesterol transport.[71] The *APOA1* gene, which encodes APOA1, is located on the long arm of chromosome 11, and a specific SNP has been identified in the promoter region (*APOA1*–75G→A).[72] It has been reported that the *APOA1*-75G/A polymorphism is related to higher high-density lipoprotein cholesterol (HDL-C) levels,[73] and a meta-analysis demonstrated the protective role of the *APOA1*-75G/A polymorphism in CVD.[65,74]

3. *APOA5* gene

APOA5, which is mainly secreted from the liver, consists of 366 amino acids.[75] It has been reported that APOA5, which is encoded by the *APOA5* gene within the *APOA1/C3/A4/A5* gene cluster on chromosome 11q23, modulates lipoprotein lipase activity[76,77] and plays roles in lipid metabolism, especially triglyceride (TG) levels.[78] Research has shown that individuals with CC homozygotes of the *APOA5* gene polymorphism (rs662799) have a 3-fold increased risk of CVD compared to those carrying the T allele. Additionally, the C allele is linked to elevated TG levels.[79] In a separate study of Caucasian obese individuals, those carrying the rs662799 C-allele of the *APOA5* gene exhibited significantly lower HDL-C levels and higher TG levels.[80] Furthermore, a meta-analysis revealed that the *APOA5* rs3135506 gene polymorphism is associated with an increased risk of CVD.[81]

4. *CETP* gene

CETP, which is synthesized in the liver, is a glycoprotein involved in the bidirectional transfer of TG and cholesteryl esters (CEs) between plasma lipoprotein particles.[82] CETP facilitates HDL-C catabolism and contributes to atherogenicity by regulating the exchange of TG and CE among lipoproteins such as APOB, LDL, VLDL, and HDL-C. It also supports reverse cholesterol transfer by transporting cholesterol esters from HDL3 to HDL2 and from peripheral tissues to the liver.[83,84] The human *CETP* gene is located on chromosome 16 in the q21 region (16q21) and contains 16 exons and 15 introns.[85] A study has shown

https://doi.org/10.12997/jla.2026.15.1.26

that increased CETP concentrations in individuals with *CETP* polymorphisms (rs247616-C, rs12720922-A, rs1968905-G) significantly reduce HDL-C and moderately increase LDL-C levels, influencing the risk of CAD.[86] The SNP rs5882 (I405V) involves the substitution of isoleucine (I) with valine (V). Consequently, the "G" allele is referred to as the "V" allele, while the "A" allele is known as the "I" allele.[87] A study exploring the relationship between cardiovascular risk, ischemic stroke formation, and CETP polymorphism found that carriers of the V allele had higher levels of plasma non-HDL, defective HDL, HDL2, HDL3, LDL, VLDL, TG, and total cholesterol (TC). The V allele was identified as a factor contributing to increased dyslipidemia.[88] Additionally, studies examining the association between *CETP* gene polymorphisms, LDL, and HDL in the development of atherosclerosis have reported conflicting results.[89]

5. Hepatic lipase (*LIPC*) gene

LIPC, which is primarily synthesized by hepatocytes and macrophages, is a 65-kD glycoprotein.[90] It plays a role in various stages of lipoprotein metabolism as a lipolytic enzyme.[91] TG and phospholipids regulate plasma concentrations by hydrolyzing plasma lipoproteins.[92] This regulatory function is influenced by the composition and quality of HDL particles.[93] In a study of male individuals with diabetes, those carrying the T allele (genotypes CT and TT) exhibited higher plasma HDL-C levels compared to those with the C allele. The influence of the *LIPC*–514C→T polymorphism on HDL-C levels was more pronounced with increased consumption of saturated fats. However, these effects of the T genotype were not observed in obese individuals.[94] A recent study identified that the *LIPC*-E97G variant contributes to familial hypercholesterolemia.[95]

6. *MTHFR* gene

MTHFR, which is a key enzyme in folate metabolism, plays a significant role in the modulation of homocysteine synthesis.[96] Homocysteine, an amino acid and homolog of cysteine, is derived from methionine. Its role in platelet activation is linked to CVD through atherosclerotic processes.[97] The *MTHFR* gene is situated at 1p36.3 on the short arm of chromosome 1.[98] Researchers have identified nine common and 34 rare mutations in the *MTHFR* gene, including the prevalent variants C677T (rs1801133), A1298C (rs1801131), and ARG184TER (rs121434294).[97] The A1298C polymorphism is believed to reduce MTHFR activity by nearly 35%.[99] The TT genotype of the *MTHFR* C677T polymorphism is recognized as a risk factor for CVD, characterized by diminished MTHFR enzyme activity and elevated homocysteine levels.[98,100] A study indicated that the rs4846049 (G>T) polymorphism in the MTHFR gene is associated with an increased risk of CVD. Additionally, the T allele has been linked to lower levels of HDL-C and APOA. Furthermore, individuals with the T allele and CVD exhibited reduced MTHFR protein levels in their blood mononuclear cells compared to those carrying the G allele.[101]

7. Arachidonate 5-lipoxygenase (*ALOX5* or *5-LO*) gene

5-LO, which is encoded by the *ALOX5* gene, is involved in the production of leukotrienes (leukotriene-B4, C4, D4, E4) from arachidonic acid.[102-104] The conversion process is facilitated by the auxiliary factor, 5-LO activating protein. Leukotriene C4 increases vascular permeability, while leukotriene B4 is implicated in inflammation.[105] Arterial inflammation plays a role in the pathophysiology of atherosclerosis. Consequently, it has been hypothesized that a polymorphism in the *5-LO* gene could be linked to the development of atherosclerosis through increased production of inflammatory leukotrienes.[106,107] In research conducted within a Chinese population, no significant association was observed between the *ALOX5AP* rs4073259

https://doi.org/10.12997/jla.2026.15.1.26

polymorphism and ischemic stroke.[108] Subsequent research indicated that *ALOX5* polymorphism may contribute to the development of atherothrombosis in middle-aged individuals.[109]

8. *FTO* gene

First identified in individuals with type 2 diabetes in Europe, the *FTO* gene is associated with body mass index (BMI), obesity, and fat mass[110,111] and is located at position 16q12.2 on chromosome 16.[112] This gene, which also has links to type 2 diabetes, is expressed in numerous tissues, including both peripheral and central areas of the brain. It encodes an alpha-ketoglutarate-dependent dioxygenase that regulates transcription and translation through the methylation of DNA/RNA.[113] Additionally, it encodes a nucleic acid demethylase (2-oxoglutarate dependent) that plays roles in fatty acid metabolism and DNA repair.[112] The most commonly studied variants of the *FTO* gene include rs9939609, rs9930506, rs17817449, and rs12149832.[110] The variant rs9939609, which has been extensively investigated in relation to body weight,[114] is associated with plasma C-reactive protein (CRP) concentration, thereby contributing to an increased cardiovascular risk.[115] According to a meta-analysis, the rs9939609 variant is linked to CVD.[111] In another clinical study, the AA genotype of rs9939609 was associated with CVD.[116] Conversely, recent research has argued that the rs17817449 variant may be associated with a reduced risk of coronary artery disease and arterial hypertension.[117]

9. *ACE* gene

ACE, which is involved in the conversion of angiotensin I to angiotensin II within the renin-angiotensin system,[118] also inhibits bradykinin.[119] The *ACE* I/D gene polymorphism (rs4340) consists of a 287 bp DNA sequence located in intron 16 of the *ACE* gene on chromosome 17q23.[119] This polymorphism plays a significant role in the pathogenesis of hypertension and CVD and is frequently studied.[120] ACE is categorized into 3 genotypes: insertion homozygous (II), insertion-deletion heterozygous (ID), and deletion homozygous (DD).[121] Research indicates that the hypertensive effect of the II genotype of the *ACE* gene, exacerbated by adiposity, is more pronounced,[122] while the DD genotype is associated with a decreased risk of CVD in the Chinese population.[123] Another study found that the *ACE* I/D polymorphism was linked to acute myocardial infarction by altering *ACE* activity, which contributes to ulceration, thrombosis, and plaque vulnerability.[120]

10. *PPAR* genes

The ligand-activated nuclear hormone receptors PPAR family consists of PPARα, PPARβ/δ, and PPARγ.[124,125] These receptors are expressed in adipose tissue and play crucial roles in various metabolic processes, including lipid metabolism, lipogenesis, adipocyte differentiation, glucose metabolism, and insulin sensitivity.[126] The *PPARA* gene is located on human chromosome 22 at locus 22q12-q13.1 and comprises eight exons that encode the PPARα protein. Common polymorphisms in *PPARA*, such as the C/G (rs1800206) and the Leu162Val amino acid substitution, have been identified and are associated with lipid metabolism.[127,128] It has been reported that single nucleotide polymorphisms in *PPAR* genes are related to obesity and cardiometabolic risk.[69,124] The *PPARA* rs1800206 C>G (L162V) polymorphism is associated with CVD, and the rs4253778 G>C (intron 7 G/C) polymorphism is related to oxidative stress and inflammation.[125] In one study, minor allele homozygotes of *PPARA* rs3856806 and rs12497191 polymorphisms exhibited a lower risk of dyslipidemia, while rs3856806 minor allele homozygotes had a lower risk of higher LDL-C.[126] In another study, *PPARA* L162V and *PPARG* C161T gene polymorphisms were found to be related to the risk of progressive acute coronary syndrome.[127]

https://doi.org/10.12997/jla.2026.15.1.26

GENE REGULATION OF THE LIPID PROFILE RESPONSE TO DIETARY INTERVENTIONS

Guidelines for the prevention of CVD recommend reducing dietary cholesterol and sodium intake, replacing saturated fats with monounsaturated or polyunsaturated fatty acids, and consuming fewer processed carbohydrates and sweetened beverages. The latest nutritional guide from the American Heart Association (AHA) highlights the importance of plant-based nutrition and the consumption of less processed foods. In this context, diets such as plant-based diets, the Mediterranean diet (MedDiet), and the Dietary Approaches to Stop Hypertension (DASH) diet are recommended for CVD prevention.[129-131] However, it has been noted that lipid profiles in response to diet vary among individuals, and genetics may play a significant role in these differences.[132,133] For this reason, recent research in nutrition has concentrated on gene expression, exploring how the synthesis of proteins interacts with bioactive components in the diet.[134] A systematic review reported that personalized diet treatments, which consider lifestyle factors, genotype, phenotype, and dietary information, improve dietary intake more effectively than traditional diet approaches.[135] Studies on gene-diet interactions of CVD risk factors are briefly summarized in **Table 1**.

Table 1. Summary of studies on gene-diet interactions of CVD risk factors

Gene	Polymorphism	Allele	Population	Country	Disease	Dietary intervention	Result/Diet response	Reference
CETP	rs3764261	T	424 adults	Spain	Individuals with MetS at risk of CVD	12 mon - MedDiet (35% fat, 22% MUFA) - Low-fat diet (28% fat, 12% MUFA)	- Carriers of the minor T allele (TT + TG) had higher plasma HDL-C concentrations and lower TG levels	Garcia-Rios et al.[84]
APOA1	At the promoter site at −75 bp (−75 base pairs)	A	1,577 adults	America	Healthy individuals	- PUFA consumption (n-3) (M>4%) - PUFA consumption (n-3) (M>8%)	- Increased HDL-C concentrations in female carriers of the A allele with PUFA intake (n-3) (energy >8%)	Ordovas et al.[92]
ALOX5	-	d5	98 adults	African Americans	Healthy individuals	5 capsules (1.0 g/capsule) per day for 6 wk - Fish oil - Corn/soybean oil	- A decrease in total TG concentration was found in individuals with the d5 genotype receiving fish oil supplements	Armstrong et al.[103]
APOA5	rs964184	G	734 adults	America	Overweight and obese individuals	2-yr weight loss diet, low fat intake (energy 20%)	- Greater reductions in TC and LDL-C in carriers of the G allele (risk allele)	Zhang et al.[136]
APOA1	rs670	A	282 adults	Spain	Obese individuals	12 wk - High-fat diet (38% carbohydrates, 24% protein, and 38% fat) - Low-fat diet (53% carbohydrates, 20% protein, and 27% fat)	- Increased HDL-C levels in A allele carriers compared to GG allele carriers after low-fat hypocaloric diet intervention	de Luis et al.[137]
LIPC	rs2070895	A	743 adults	America	Overweight and obese individuals	2-yr weight loss diet - 20%, 15% and 65% - 20%, 25% and 55% - 40%, 15% and 45% - 40%, 25% and 35%	- Further reductions in TC and LDL-C with low-fat diet in carriers of the A allele - Increase in HDL-C	Xu et al.[138]
LIPC	rs1800588	C	42 adults	Spain	Healthy individuals	4 wk - High-fat Western diet (39% fat) - Low-fat traditional Spanish diet (20% fat)	- In carriers of major alleles (CC/CT), increase in HDL-C levels following Western diet compared to Spanish diet - No change in minor allele (TT) carriers	Smith et al.[139]
CETP	rs3764261	C	732 (pounds lost) 171 (direct)	America	Overweight and obese individuals	2-yr weight loss diet - High fat intake (energy 40%)	- Carriers of the C allele with a high-fat diet showed a greater increase in HDL-C and a greater decrease in TG levels	Qi et al.[140]

(continued to the next page)

https://doi.org/10.12997/jla.2026.15.1.26

Table 1. (Continued) Summary of studies on gene-diet interactions of CVD risk factors

Gene	Polymorphism	Allele	Population	Country	Disease	Dietary intervention	Result/Diet response	Reference
ACE	rs4343	G	46 adults	United Kingdom	Healthy, non-obese individuals	6-wk high-saturated-fat diet	- 2-fold increase in ACE concentrations and higher systolic blood pressure in individuals with the GG allele	Schüler et al.[141]
TCF7L2	rs7903146	T	7,018 adults	Spain	Individuals with type 2 diabetes and 3 or more cardiovascular risk factors (hypertension, dyslipidemia, BMI ≥25 kg/m^2, smoking, or a family history of CVD; 1 of the 2 criteria)	- MedDiet with 50 mL/day of extra virgin olive oil - MedDiet with 30 g/day mixed nuts	- Reduced stroke risk and decreased TC, LDL-C, and TG when adherence to the MedDiet increased in individuals with the TT genotype	Corella et al.[142]
MLXIPL	rs3812316	G	7,166 adults	Spain	Individuals at risk of CVD	MedDiet (median 4.8 yr follow-up)	- Reduced risk of myocardial infarction in carriers of the G allele compared to carriers of the C allele	Ortega-Azorín et al.[143]
LPL	rs13702	C	7,187 adults	Spain	Individuals at risk of CVD	MedDiet (median 4.8 yr follow-up)	- Further reductions in TG and reduced risk of stroke in carriers of the C allele after MedDiet intervention	Corella et al.[144]
APOA1	rs670	A	82 adults	Spain	Obese individuals	Mediterranean type hypocaloric diet (500 kcal per day for 12 wk)	- Decreases in TC and LDL-C levels in carriers of the A allele	de Luis et al.[145]
TNF-α	rs1800629, rs1799964	A	507 adults	Spain	Individuals with MetS	12 mon - MedDiet (35% fat, 22% MUFA) - Low-fat diet (28% fat, 12% MUFA)	- Decrease in TG and hsCRP in individuals with the G/G allele after 12 mon of MedDiet intervention	Gomez-Delgado et al.[146]
APOE	rs429358 and rs7412	ε4	1466 adults	Europe	Healthy individuals	Gene-based personalized dietary advice	- Decrease in TC concentrations was significantly greater in ε4+ than in ε4– participants	Fallaize et al.[147]
APOE	rs1064725	T	120 adults	Caucasia	Individuals with a moderate risk of CVD	16-wk isoenergetic diet - Total oil (energy 36%) - SFAs (17:11:4) - MUFAs (9:19:4) - n-6 PUFAs (9:13:10)	- Significant reduction in TC after consumption of MUFA-rich diets compared to SFA or n-6 PUFA diets in individuals with the TT allele	Shatwan et al.[148]

CVD, cardiovascular disease; *CETP*, cholesterol ester transfer protein; MetS, metabolic syndrome; MedDiet, Mediterranean diet; MUFA, monounsaturated fatty acid; HDL-C, high-density lipoprotein cholesterol; TG, triglyceride; *APOA1*, apolipoprotein A1; PUFA, polyunsaturated fatty acid; *ALOX5* or *5-LO*, arachidonate 5-lipoxygenase; *APOA5*, apolipoprotein A5; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; *LIPC*, hepatic lipase; *ACE*, angiotensin-converting enzyme; *TCF7L2*, transcription factor 7-like 2; BMI, body mass index; *MLXIPL*, max-like protein X interacting protein-like; *LPL*, lipoprotein lipase; *TNF-α*, tumor necrosis factor-α; hsCRP, high-sensitivity C-reactive protein; *APOE*, apolipoprotein E; SFA, saturated fatty acid.

1. High- and low-fat diets

In a study examining overweight and obese individuals with the rs964184 polymorphism in the *APOA5* gene, those on a low-fat diet (20% energy from fat) who were also carriers of the risk allele (G allele) exhibited lower LDL and TC concentrations compared to non-carriers after 2 years of dietary intervention. Conversely, carriers of the risk allele who consumed a high-fat diet (40% energy from fat) showed a more pronounced increase in HDL-C response. No significant interactions were observed between protein intake and the *APOA5* rs964184 genotype regarding changes in lipid concentrations.[136] These results highlight that gene-diet interactions affecting blood lipid profiles become apparent after long-term interventions. It has been noted that variations in HDL-C concentrations are linked to the *APOA5* genotype, although the underlying mechanisms remain unclear. Another study investigated the impact of 2 different hypocaloric diets on metabolic changes and lipid profiles in individuals with the *APOA1* rs670 gene polymorphism. This study included obese participants who were randomly assigned to either a low-fat diet or a high-fat diet for 12 weeks. Measurements taken after the dietary interventions showed reductions in BMI, waist circumference, body weight, leptin levels, fat mass, and systolic

https://doi.org/10.12997/jla.2026.15.1.26

blood pressure. Following the low-fat hypocaloric diet, individuals carrying the A allele experienced an increase in HDL-C levels compared to those with the GG allele.[137]

In a study examining the relationship between the −541C/T polymorphism in the *LIPC* gene and dietary fat, individuals with the T allele who consumed a diet with less than 30% of energy from fat exhibited higher HDL-C levels. However, when total fat intake was 30% or more of energy, no difference was observed in individuals with the C allele, while those with the TT genotype had lower HDL-C concentrations.[149] Another study investigated the effects of a 2-year dietary intervention (high-fat, 40%; low-fat, 20%) on the lipid profiles of overweight and obese individuals with the *LIPC* rs2070895 polymorphism. This study found that A allele carriers experienced a decrease in plasma LDL and TC levels and an increase in HDL-C concentrations when following a low-fat diet, compared to G allele carriers. Conversely, A allele carriers on a high-fat diet experienced adverse effects on LDL and TC levels, with no significant change in HDL-C levels.[138] According to that study by Xu et al.,[138] carriers of the A allele may experience better modulation of lipid profiles with a diet low in fat (20%) and high in carbohydrates (55%–65%). Another study focused on the effects of the rs1800588 polymorphism in the *LIPC* gene on blood glucose and lipid responses in Hispanic individuals following a low-fat traditional Hispanic diet versus a Western diet. The results indicated that individuals with the C allele (CC+CT) who consumed a Western diet had higher HDL-C levels. In contrast, those with the T allele did not show a significant increase in HDL-C levels, nor a decrease. Additionally, the same polymorphism, TG, HDL-C, and dietary fat quality were reassessed using data from the Boston Puerto Rico Health Study. It was found that saturated fat consumption was negatively associated with TG and HDL-c levels in individuals with the TT genotype.[139] These studies showed that *LIPC* polymorphism affects the response to dietary intake.

In a study utilizing data from 2 independent 2-year randomized controlled trials—Dietary Intervention Randomized Controlled Trial (DIRECT) and Preventing Excess Weight Using New Dietary Strategies (POUNDS LOST)— researchers evaluated the impact of the *CETP* rs3764261 polymorphism on blood lipid responses to dietary interventions. In the POUNDS LOST study, which involved overweight or obese participants, those carrying the C allele of the *CETP* rs3764261 polymorphism experienced a greater reduction in TG levels and an increase in HDL-C over 6 months when following a high-fat diet (40% of energy from fat) compared to a low-fat diet (20% of energy from fat). Similarly, the DIRECT study showed comparable changes in TG and HDL-C levels.[140] No significant differences were observed between individuals with AA and CA genotypes. The findings indicate that individuals with the *CETP* rs3764261 CC genotype may see more pronounced improvements in TG and HDL-C levels when following a low-carbohydrate/high-fat weight loss diet. Another study explored the effects of a high-saturated isocaloric diet on ACE levels. Participants initially followed a high-carbohydrate, low-fat diet for 6 weeks, then switched to a high-saturated fat diet for another 6 weeks under isocaloric conditions. Consumption of the high-fat diet led to a 15% increase in circulating ACE concentration due to increased *ACE* gene expression. Individuals with the GG genotype exhibited higher baseline ACE concentrations, which doubled following the high-fat diet compared to those carrying the A allele. Additionally, higher systolic blood pressure was noted in individuals with the GG genotype than in those with AA or AG genotypes.[141] The study concluded that individuals with the *ACE* rs4343 GG genotype who consume a high-saturated fat diet may face increased CVD risk.

https://doi.org/10.12997/jla.2026.15.1.26

JLA Journal of Lipid and Atherosclerosis

2. MedDiet

The MedDiet has been shown to play a protective role in CVD, with benefits including limiting oxidation, protecting membrane fluidity, enhancing nitric oxide production, balancing meal distribution, modulating microbial activity, and influencing gene expression.[150] One study assessed the impact of consuming a MedDiet (35% fat, 22% MUFA) versus a low-fat diet (28% fat, 12% MUFA) over one year. It focused on how these diets interact with the rs3764261 SNP at the CETP locus to affect lipid metabolism in individuals with metabolic syndrome (MetS) who are at high risk for CVD. After one year, individuals carrying the T allele (TT+TG) exhibited lower plasma TG concentrations and higher HDL-C levels compared to those with the GG genotype.[84] In individuals with the *TCF7L2* rs7903146 (C>T) polymorphism, those with the TT genotype displayed higher fasting glucose levels and an increased risk of stroke compared to those with the C allele. However, as adherence to the diet increased, the risk of stroke diminished, and levels of TC, LDL-C, and TG decreased. No effect on myocardial infarction was observed.[142] Notably, in the control group (which received a low-fat diet without the MedDiet), individuals with the TT allele had a higher incidence of stroke than those with the CC allele, whereas adherence to the MedDiet for 4.8 years was associated with a reduced incidence of stroke. The study also explored the impact of the max-like protein X interacting protein-like (*MLXIPL*) rs3812316 polymorphism on dietary response and its association with CVD in individuals at risk, as part of the PREDIMED study. The *MLXIPL*-rs3812316 polymorphism has been linked to lower TG levels and a reduced risk of hypertriglyceridemia. These protective effects increased with greater adherence to the MedDiet and were associated with a lower risk of myocardial infarction in carriers of the G allele than in those with the CC genotype.[143] Another segment of the PREDIMED study involving 7187 participants evaluated the association of the lipoprotein lipase (*LPL*) gene variant (rs13702T>C) with CVD incidence and response to the MedDiet intervention. The rs13702T>C polymorphism was associated with lower TG levels in carriers of the C allele, who also experienced greater reductions in TG following the MedDiet intervention, which is rich in monounsaturated and unsaturated fats. Although the polymorphism was linked to a lower risk of stroke, this association became more statistically significant with the MedDiet intervention.[144] In a separate study involving obese individuals, the rs670 *APOA1* gene polymorphism was evaluated after a 12-week Mediterranean-type hypocaloric diet (500 kcal per day). It was found that the A allele (GG, GA+AA) was the risk allele. Post-dietary intervention, BMI, fat mass, waist circumference, and body weight decreased in both A and G allele carriers, with more pronounced effects in A allele carriers. Additionally, there was a decrease in insulin resistance, insulin levels, homeostatic model assessment insulin resistance, LDL-C, and TC in individuals with the A allele.[145]

Inflammation has been reported to be an independent risk factor for the development and progression of both cardiac and vascular diseases.[151,152] A study investigated the effects of a low-fat diet and a MedDiet on aging-related processes such as inflammation, oxidative stress, and leukocyte telomere length (LTL) in individuals with coronary heart disease (CHD) who had *SIRT1* rs7069102 and rs1885472 polymorphisms. Subjects with the GG genotype who were randomized to the low-fat diet experienced a significant reduction in lipid peroxidation products and tumor necrosis factor-α (TNF-α) levels compared to their baseline levels and those in subjects with the CG+CC genotype. Additionally, an increase in the ratio of reduced to oxidized glutathione was observed. Stabilization in LTL was noted in GG carriers compared to C allele carriers. In contrast, individuals assigned to the MedDiet showed a decrease in telomere length across both genotypes, with no significant changes in CRP and TNF-α levels.[153] This study demonstrated the beneficial effects of the low-fat diet

https://doi.org/10.12997/jla.2026.15.1.26

JLA Journal of Lipid and Atherosclerosis

in individuals with CHD and the *SIRT1* rs7069102 polymorphism. Another study assessed the associations of polymorphisms (rs1800629, rs1799964) in the *TNFA* gene with responses to a low-fat diet versus a MedDiet in individuals with MetS. Conducted with 507 participants from the CORDIOPREV clinical study, the initial findings showed that plasma CRP and both fasting and postprandial TG levels were higher in individuals with the GG genotype than in those carrying the A allele. After a 1-year dietary intervention, plasma CRP and TG levels decreased in carriers of the GG genotype compared to those with the A allele.[146] These results suggest that rs1800629 in the *TNFA* gene modifies TG metabolism and inflammatory response with the MedDiet in individuals with MetS.

3. Other types of diets and dietary supplements

In a study utilizing data from the Food4Me pan-European personalized nutrition study, individuals carrying the *APOE* ε4 allele exhibited higher TC levels. It was also observed that gene-based personalized dietary advice significantly promoted the reduction of saturated fat consumption compared to non-gene-based personalized diet therapy.[147] Another study assessed the impact of personalized nutrition therapy, identifying the T allele as the risk allele for the *MTHFR* gene (CT and TT genotypes), and the ε4 allele as the risk allele for the *APOE* gene (ε3/ε4 and ε4/ε4 genotypes). Participants received guidance on increasing their folate intake and reducing their saturated fat intake (folate >200 μg/day; saturated fat <11% TEI-UK available data). Following the intervention, participants with the genetic risk reduced their saturated fat consumption to recommended levels, whereas the risk-free genotype group also reduced their intake, but their average consumption remained above the recommended level.[154] This study demonstrated that incorporating genotype-based personalized nutritional recommendations into dietary behavior interventions can lead to positive changes in dietary behavior. In a cross-sectional study investigating the influence of *CETP* TaqB1 polymorphism on CVD risk factors among individuals with diabetes, the *CETP* Taq1B B1 allele was found to be protective against CVD risk in those with high dietary insulin index and load.[132] Another cross-sectional study conducted in Iran explored the impact of polymorphisms in the *CETP* gene (rs5882 and rs3764261) on the serum lipid profile response to diet over a 3.6-year follow-up period. In this study, higher fish intake was associated with reduced TC in carriers of the A allele in the rs3764261 polymorphism compared to those with the CC genotype. Additionally, G allele carriers of rs5882 who consumed a low-fat and high-carbohydrate diet had better TG levels than individuals with the AA homozygous allele. Furthermore, carriers of the A allele of rs3764261 exhibited higher HDL-C and lower TG levels compared to those with the CC genotype.[133]

In a study evaluating the impact of CVD-related genes such as *APOE* and cholesterol 7 alpha-hydroxylase (*CYP7A1*) on LDL-c response to plant sterol (PS) supplementation, participants received either 2 g of PS per day or a placebo for 28 days. The results showed a dose-dependent reduction in LDL-C levels among individuals carrying the G allele, while no change was observed in those with the TT genotype.[155] Another study analyzed three isoenergetic diets rich in SFA, n-6 polyunsaturated fatty acids (PUFA), or MUFA, which were given for 16 weeks to examine the effect of dietary interventions on blood lipid profile in individuals with moderate cardiovascular risk with *LPL* and *APOE* single nucleotide polymorphisms. This study found a significant reduction in TC after consumption of MUFA-rich diets compared to those rich in n-6 PUFA or SFA, particularly in individuals with the TT allele of the *APOE* SNP rs1064725. In carriers of the G allele of the *LPL* SNP, a decrease in LDL-C levels was observed in the group consuming a diet rich in n-6 PUFA, although this change was not statistically significant.[148] The study noted that TT homozygotes were more

https://doi.org/10.12997/jla.2026.15.1.26

JLA Journal of Lipid and Atherosclerosis

sensitive to dietary fat composition. APOA1, a protein encoded by the human *APOA1* gene, plays a role in lipid metabolism and the risk of CHD. A study investigating the influence of dietary fat on HDL-C concentrations in individuals with polymorphisms in the *APOA1* gene promoter found that female participants with the A allele had lower HDL-C concentrations compared to G/G homozygotes. Regression model results indicated that when PUFA intake was less than 4% of energy, HDL-C concentrations were approximately 14% higher in individuals with the G/G genotype than in those carrying the A allele. Conversely, with a PUFA intake greater than 8%, HDL-C levels were 13% higher in individuals with the A allele than in G/G homozygotes. This suggests that female individuals with the A allele might benefit from a high-PUFA diet in terms of reducing CVD risk.[92] In a separate study involving Taiwanese individuals with the rs1801133 polymorphism in the *MTHFR* gene, the effects of a vegetarian diet and exercise levels on HDL-C levels were examined. This study of healthy adults showed that increased exercise time per week was associated with higher HDL-C levels, while a vegetarian diet was linked to lower HDL-C levels. Combining a vegetarian diet with exercise led to a decrease in HDL-C of 6.5552 mg/dL in individuals with the GG genotype and a decrease of 2.8668 mg/dL in those with the GA+AA genotype. These results indicate that a vegetarian diet tends to lower HDL-C levels, regardless of the rs1801133 genotype, and that higher exercise durations correlate with increased HDL-C levels in individuals carrying the A allele (GA+AA).[156]

It is known that dietary responses can be influenced by gene polymorphism. A study was conducted to determine if fish oil and corn/soybean oil supplements impact plasma lipoprotein and lipid concentrations, blood pressure, heart rate, and erythrocyte PUFA composition in individuals with different *ALOX5* gene variants (genotypes = dd, d5, and 55). Participants were administered 5 g/day of either fish oil or corn/soybean oil for 6 weeks. At the conclusion of the intervention, a significant reduction in total TG concentration was observed in participants who received fish oil supplements compared to those who received corn/soybean oil supplements. Furthermore, this effect was exclusive to individuals with the d5 genotype and was not observed in those with the dd or 55 genotypes. Additionally, HDL particle concentration decreased with fish oil in individuals with d5 and 55 genotypes relative to those given corn/soybean oil, but no change was noted in those with the dd genotype. No differences were observed in heart rate, blood pressure, or LDL particles.[103] This study demonstrated that responses to fish oil supplements are affected by the *ALOX5* genotype.

CONCLUSION

In the field of CVDs, ongoing GWAS continue to uncover and identify new loci, with numerous investigations exploring how these polymorphisms interact with various diets. For instance, the *CETP* gene polymorphism is linked to responses to the MedDiet, leading to changes in cholesterol and TG levels. Similarly, polymorphisms in the *APOA1* gene may affect HDL-C responses to dietary fats. Additionally, polymorphisms in the *APOE*, *LIPC*, and *APOA5* genes can modify the impact of high-fat or low-fat diets on lipid profiles. These findings underscore the importance of tailoring dietary recommendations to individual genetic profiles. Despite the growing body of gene studies, research on the interactions between diet and genes remains relatively scarce. There is a pressing need for more research to evaluate the benefits and drawbacks of studying single genes versus multiple genes in conjunction. Moreover, considering the potential effects of gene-drug interactions, such as those involving bioactive food components, could enhance the efficacy of gene-diet studies. Furthermore, the impact

https://doi.org/10.12997/jla.2026.15.1.26

JLA Journal of Lipid and Atherosclerosis

of genetic information on an individual's nutritional status is still unclear. It is crucial to recognize that individuals lacking risk alleles might be inclined to consume more unhealthy foods, while those with risk alleles may require psychological evaluation.

In conclusion, understanding the interactions between genetic makeup and diet is essential for developing personalized nutrition strategies that can significantly reduce the risk of CVDs. Future strategies should focus on collecting genetic information to build databases, enhancing public and healthcare professional awareness through education on nutrigenetics, improving access to genetic testing, conducting multidisciplinary research, and prioritizing long-term clinical studies that emphasize collaboration. These initiatives are poised to contribute to more effective and reliable solutions in the field.

REFERENCES

1. Sharifi-Rad J, Rodrigues CF, Sharopov F, Docea AO, Can Karaca A, Sharifi-Rad M, et al. Diet, lifestyle and cardiovascular diseases: linking pathophysiology to cardioprotective effects of natural bioactive compounds. Int J Environ Res Public Health 2020;17:2326. PUBMED | CROSSREF
2. Hsu CN, Hou CY, Hsu WH, Tain YL. Cardiovascular diseases of developmental origins: preventive aspects of gut microbiota-targeted therapy. Nutrients 2021;13:2290. PUBMED | CROSSREF
3. Dubois-Deruy E, Peugnet V, Turkieh A, Pinet F. Oxidative stress in cardiovascular diseases. Antioxidants 2020;9:864. PUBMED | CROSSREF
4. Szczepańska E, Białek-Dratwa A, Janota B, Kowalski O. Dietary therapy in prevention of cardiovascular disease (CVD)-tradition or modernity? A review of the latest approaches to nutrition in CVD. Nutrients 2022;14:2649. PUBMED | CROSSREF
5. Brandhorst S, Longo VD. Dietary restrictions and nutrition in the prevention and treatment of cardiovascular disease. Circ Res 2019;124:952-965. PUBMED | CROSSREF
6. Benjamin EJ, Virani SS, Callaway CW, Chamberlain AM, Chang AR, Cheng S, et al. Heart disease and stroke statistics—2018 update: a report from the American Heart Association. Circulation 2018;137:e67-e492. PUBMED | CROSSREF
7. Kraus WE, Powell KE, Haskell WL, Janz KF, Campbell WW, Jakicic JM, et al. Physical activity, all-cause and cardiovascular mortality, and cardiovascular disease. Med Sci Sports Exerc 2019;51:1270-1281. PUBMED | CROSSREF
8. World Health Organization. Cardiovascular disease [Internet]. Geneva: World Health Organization; [cited 2022 Dec 18]. Available from: https://www.who.int/health-topics/cardiovascular-diseases#tab=tab_1.
9. Phillips CM. Nutrigenetics and metabolic disease: current status and implications for personalised nutrition. Nutrients 2013;5:32-57. PUBMED | CROSSREF
10. Rychter AM, Ratajczak AE, Zawada A, Dobrowolska A, Krela-Kaźmierczak I. Non-systematic review of diet and nutritional risk factors of cardiovascular disease in obesity. Nutrients 2020;12:814. PUBMED | CROSSREF
11. Lombardi R, Iuculano F, Pallini G, Fargion S, Fracanzani AL. Nutrients, genetic factors, and their interaction in non-alcoholic fatty liver disease and cardiovascular disease. Int J Mol Sci 2020;21:8761. PUBMED | CROSSREF
12. Peña-Romero AC, Navas-Carrillo D, Marín F, Orenes-Piñero E. The future of nutrition: nutrigenomics and nutrigenetics in obesity and cardiovascular diseases. Crit Rev Food Sci Nutr 2018;58:3030-3041. PUBMED | CROSSREF
13. Konstantinidou V, Daimiel L, Ordovás JM. Personalized nutrition and cardiovascular disease prevention: from Framingham to PREDIMED. Adv Nutr 2014;5:368S-371S. PUBMED | CROSSREF
14. Jellinger PS, Handelsman Y, Rosenblit PD, Bloomgarden ZT, Fonseca VA, Garber AJ, et al. American Association of Clinical Endocrinologists and American College of Endocrinology guidelines for management of dyslipidemia and prevention of cardiovascular disease. Endocr Pract 2017;23:1-87. PUBMED | CROSSREF
15. Anderson TJ, Grégoire J, Pearson GJ, Barry AR, Couture P, Dawes M, et al. 2016 Canadian Cardiovascular Society guidelines for the management of dyslipidemia for the prevention of cardiovascular disease in the adult. Can J Cardiol 2016;32:1263-1282. PUBMED | CROSSREF

https://doi.org/10.12997/jla.2026.15.1.26

16. Mozaffarian D, Ludwig DS. The 2015 US dietary guidelines: lifting the ban on total dietary fat. JAMA 2015;313:2421-2422. PUBMED | CROSSREF
17. Perk J, De Backer G, Gohlke H, Graham I, Reiner Z, Verschuren M, et al. European Guidelines on cardiovascular disease prevention in clinical practice (version 2012). The Fifth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of nine societies and by invited experts). Eur Heart J 2012;33:1635-1701. PUBMED | CROSSREF
18. Eckel RH, Jakicic JM, Ard JD, de Jesus JM, Houston Miller N, Hubbard VS, et al. 2013 AHA/ACC guideline on lifestyle management to reduce cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation 2014;129:S76-S99. PUBMED | CROSSREF
19. Ferguson LR, De Caterina R, Görman U, Allayee H, Kohlmeier M, Prasad C, et al. Guide and position of the international society of nutrigenetics/nutrigenomics on personalised nutrition: part 1-fields of precision nutrition. J Nutrigenet Nutrigenomics 2016;9:12-27. PUBMED | CROSSREF
20. Barrea L, Annunziata G, Bordoni L, Muscogiuri G, Colao A, Savastano S, et al. Nutrigenetics-personalized nutrition in obesity and cardiovascular diseases. Int J Obes Suppl 2020;10:1-13. PUBMED | CROSSREF
21. Desjardins LC, Vohl MC. Precision nutrition for cardiovascular disease prevention. Lifestyle Genom 2023;16:73-82. CROSSREF
22. Eichner JE, Dunn ST, Perveen G, Thompson DM, Stewart KE, Stroehla BC. Apolipoprotein E polymorphism and cardiovascular disease: a HuGE review. Am J Epidemiol 2002;155:487-495. PUBMED | CROSSREF
23. Klerk M, Verhoef P, Clarke R, Blom HJ, Kok FJ, Schouten EG, et al. MTHFR 677C-->T polymorphism and risk of coronary heart disease: a meta-analysis. JAMA 2002;288:2023-2031. PUBMED | CROSSREF
24. Voruganti VS. Nutritional genomics of cardiovascular disease. Curr Genet Med Rep 2018;6:98-106. PUBMED | CROSSREF
25. Pérez-Beltrán YE, González-Becerra K, Rivera-Iñiguez I, Martínez-López E, Ramos-Lopez O, Alcaraz-Mejía M, et al. A nutrigenetic strategy for reducing blood lipids and low-grade inflammation in adults with obesity and overweight. Nutrients 2023;15:4324. PUBMED | CROSSREF
26. Pérez-Beltrán YE, Rivera-Iñiguez I, Gonzalez-Becerra K, Pérez-Naitoh N, Tovar J, Sáyago-Ayerdi SG, et al. Personalized dietary recommendations based on lipid-related genetic variants: a systematic review. Front Nutr 2022;9:830283. PUBMED | CROSSREF
27. Cai J, Liu Q, Liu S, Mai T, Xu M, He H, et al. Associations between apolipoprotein E gene polymorphism, diet and dyslipidemia in a Yao minority area, China. J Am Nutr Assoc 2022;41:690-696. PUBMED | CROSSREF
28. Zhang S, Chen S, He K, Liu J, Su X, Li W, et al. The interaction of dietary patterns and genetic variants on the risk of cardiovascular diseases in chinese patients with type 2 diabetes. Mol Nutr Food Res 2023;67:e2300332. PUBMED | CROSSREF
29. Mollahosseini M, Rahimi MH, Yekaninejad MS, Maghbooli Z, Mirzaei K. Dietary patterns interact with chromosome 9p21 rs1333048 polymorphism on the risk of obesity and cardiovascular risk factors in apparently healthy Tehrani adults. Eur J Nutr 2020;59:35-43. PUBMED | CROSSREF
30. Ceci FM, Ceccanti M, Petrella C, Vitali M, Messina MP, Chaldakov GN, et al. Alcohol drinking, apolipoprotein polymorphisms and the risk of cardiovascular diseases. Curr Neurovasc Res 2021;18:150-161. PUBMED | CROSSREF
31. Montes-de-Oca-García A, Perez-Bey A, Velázquez-Díaz D, Corral-Pérez J, Opazo-Díaz E, Rebollo-Ramos M, et al. Influence of *ACE* gene I/D polymorphism on cardiometabolic risk, maximal fat oxidation, cardiorespiratory fitness, diet and physical activity in young adults. Int J Environ Res Public Health 2021;18:3443. PUBMED | CROSSREF
32. Park S, Kang S. A minor allele of the haplotype located in the 19q13 loci is associated with a decreased risk of hyper-LDL-cholesterolemia, and a balanced diet and high protein intake can reduce the risk. Lipids Health Dis 2020;19:178. PUBMED | CROSSREF
33. Corcuff JB, Merched AJ. Chapter 3 - Nutrigenomics and nutrigenetics: the basis of molecular nutrition. In: Malavolta M, Mocchegiani E, editors. Molecular basis of nutrition and aging. Boston: Elsevier; 2016. p.21-29. CROSSREF
34. Rodriguez–Leyva D, Malik A, Tappia P. Gender-related gene expression in response to dietary fatty acids and predisposition to atherosclerosis and cardiovascular disease. Clin Lipidol 2011;6:653-664. CROSSREF
35. Lovegrove JA, Gitau R. Personalized nutrition for the prevention of cardiovascular disease: a future perspective. J Hum Nutr Diet 2008;21:306-316. PUBMED | CROSSREF
36. Uthpala TG, Fernando HN, Thibbotuwawa A, Jayasinghe M. Importance of nutrigenomics and nutrigenetics in food Science. MOJ Food Process Technols 2020;8:114-119. CROSSREF

37. Joffe YT, Houghton CA. A novel approach to the nutrigenetics and nutrigenomics of obesity and weight management. Curr Oncol Rep 2016;18:43. PUBMED | CROSSREF

38. Bhori M, Rastogi V, Tungare K, Marar T. A review on interplay between obesity, lipoprotein profile and nutrigenetics with selected candidate marker genes of type 2 diabetes mellitus. Mol Biol Rep 2022;49:687-703. PUBMED | CROSSREF

39. Franzago M, Santurbano D, Vitacolonna E, Stuppia L. Genes and diet in the prevention of chronic diseases in future generations. Int J Mol Sci 2020;21:2633. PUBMED | CROSSREF

40. Bouchard C, Ordovas JM. Fundamentals of nutrigenetics and nutrigenomics. Prog Mol Biol Transl Sci 2012;108:1-15. PUBMED | CROSSREF

41. Roa-Díaz ZM, Teuscher J, Gamba M, Bundo M, Grisotto G, Wehrli F, et al. Gene-diet interactions and cardiovascular diseases: a systematic review of observational and clinical trials. BMC Cardiovasc Disord 2022;22:377. PUBMED | CROSSREF

42. Ordovas JM. Gene-diet interactions and cardiovascular diseases: Saturated and monounsaturated fat. In: De Caterina R, Martinez JA, Kohlmeier M, editors. Principles of nutrigenetics and nutrigenomics: fundamentals of individualized nutrition. London: Academic Press; 2020. p.211-222. CROSSREF

43. Rather RA, Dhawan V. Genetic markers: potential candidates for cardiovascular disease. Int J Cardiol 2016;220:914-923. PUBMED | CROSSREF

44. Gianfagna F, Cugino D, Santimone I, Iacoviello L. From candidate gene to genome-wide association studies in cardiovascular disease. Thromb Res 2012;129:320-324. PUBMED | CROSSREF

45. Cambien F, Poirier O, Lecerf L, Evans A, Cambou JP, Arveiler D, et al. Deletion polymorphism in the gene for angiotensin-converting enzyme is a potent risk factor for myocardial infarction. Nature 1992;359:641-644. PUBMED | CROSSREF

46. Franchini M, Peyvandi F, Mannucci PM. The genetic basis of coronary artery disease: from candidate genes to whole genome analysis. Trends Cardiovasc Med 2008;18:157-162. PUBMED | CROSSREF

47. Vrablik M, Dlouha D, Todorovova V, Stefler D, Hubacek JA. Genetics of cardiovascular disease: how far are we from personalized CVD risk prediction and management? Int J Mol Sci 2021;22:4182. PUBMED | CROSSREF

48. Bailey JN, Pericak-Vance MA, Haines JL. The impact of the human genome project on complex disease. Genes (Basel) 2014;5:518-535. PUBMED | CROSSREF

49. Uffelmann E, Huang QQ, Munung NS, De Vries J, Okada Y, Martin AR, et al. Genome-wide association studies. Nat Rev Methods Primers 2021;1:59. CROSSREF

50. Mauersberger C, Schunkert H, Sager HB. Inflammation-related risk loci in genome-wide association studies of coronary artery disease. Cells 2021;10:440. PUBMED | CROSSREF

51. Karki R, Pandya D, Elston RC, Ferlini C. Defining "mutation" and "polymorphism" in the era of personal genomics. BMC Med Genomics 2015;8:37. PUBMED | CROSSREF

52. Marth GT, Korf I, Yandell MD, Yeh RT, Gu Z, Zakeri H, et al. A general approach to single-nucleotide polymorphism discovery. Nat Genet 1999;23:452-456. PUBMED | CROSSREF

53. LaFramboise T. Single nucleotide polymorphism arrays: a decade of biological, computational and technological advances. Nucleic Acids Res 2009;37:4181-4193. PUBMED | CROSSREF

54. Dimitriou ME, Dedoussis GV. Gene–diet interactions in cardiovascular disease. Curr Nutr Rep 2012;1:153-160. CROSSREF

55. Erdmann J, Kessler T, Munoz Venegas L, Schunkert H. A decade of genome-wide association studies for coronary artery disease: the challenges ahead. Cardiovasc Res 2018;114:1241-1257. PUBMED | CROSSREF

56. Kessler T, Vilne B, Schunkert H. The impact of genome-wide association studies on the pathophysiology and therapy of cardiovascular disease. EMBO Mol Med 2016;8:688-701. PUBMED | CROSSREF

57. Kessler T, Schunkert H. Coronary artery disease genetics enlightened by genome-wide association studies. JACC Basic Transl Sci 2021;6:610-623. PUBMED | CROSSREF

58. Smith JG, Newton-Cheh C. Genome-wide association studies of late-onset cardiovascular disease. J Mol Cell Cardiol 2015;83:131-141. PUBMED | CROSSREF

59. Gök Ö, Aslan A, Erman O. İnsan ENCODE, HapMap ve 1000 Genom Projeler. Erciyes Üniversitesi Fen Bilimleri Enstitüsü Fen Bilimleri Dergisi 2017;33:35-42.

60. Lewis CM, Vassos E. Polygenic risk scores: from research tools to clinical instruments. Genome Med 2020;12:44. PUBMED | CROSSREF

61. Thanassoulis G, Peloso GM, Pencina MJ, Hoffmann U, Fox CS, Cupples LA, et al. A genetic risk score is associated with incident cardiovascular disease and coronary artery calcium: the Framingham Heart Study. Circ Cardiovasc Genet 2012;5:113-121. PUBMED | CROSSREF

62. Inouye M, Abraham G, Nelson CP, Wood AM, Sweeting MJ, Dudbridge F, et al. Genomic risk prediction of coronary artery disease in 480,000 adults: implications for primary prevention. J Am Coll Cardiol 2018;72:1883-1893. PUBMED | CROSSREF

63. Ye Y, Chen X, Han J, Jiang W, Natarajan P, Zhao H. Interactions between enhanced polygenic risk scores and lifestyle for cardiovascular disease, diabetes, and lipid levels. Circ Genom Precis Med 2021;14:e003128. PUBMED | CROSSREF

64. Khanna NN, Singh M, Maindarkar M, Kumar A, Johri AM, Mentella L, et al. Polygenic Risk Score For Cardiovascular Diseases In Artificial Intelligence Paradigm: A Review. J Korean Med Sci 2023;38:e395. PUBMED | CROSSREF

65. Chen Z, Schunkert H. Genetics of coronary artery disease in the post-GWAS era. J Intern Med 2021;290:980-992. PUBMED | CROSSREF

66. Chouinard-Watkins R, Plourde M. Fatty acid metabolism in carriers of apolipoprotein E epsilon 4 allele: is it contributing to higher risk of cognitive decline and coronary heart disease? Nutrients 2014;6:4452-4471. PUBMED | CROSSREF

67. Hietaranta-Luoma HL, Luomala HT, Puolijoki H, Hopia A. Using ApoE genotyping to promote healthy lifestyles in Finland–psychological impacts: randomized controlled trial. J Genet Couns 2015;24:908-921. PUBMED | CROSSREF

68. Li MY, Kwok MK, Schooling CM. Investigating effects of plasma apolipoprotein E on ischemic heart disease using Mendelian randomization study. Nutrients 2021;13:2215. PUBMED | CROSSREF

69. Ferguson JF, Allayee H, Gerszten RE, Ideraabdullah F, Kris-Etherton PM, Ordovás JM, et al. Nutrigenomics, the microbiome, and gene-environment interactions: new directions in cardiovascular disease research, prevention, and treatment: a scientific statement from the American Heart Association. Circ Cardiovasc Genet 2016;9:291-313. PUBMED | CROSSREF

70. Endres K. Apolipoprotein A1, the neglected relative of apolipoprotein E and its potential role in Alzheimer's disease. Neural Regen Res 2021;16:2141-2148. PUBMED | CROSSREF

71. Liao B, Cheng K, Dong S, Liu H, Xu Z. Effect of apolipoprotein A1 genetic polymorphisms on lipid profiles and the risk of coronary artery disease. Diagn Pathol 2015;10:102. PUBMED | CROSSREF

72. Ordovas JM. Genetic interactions with diet influence the risk of cardiovascular disease. Am J Clin Nutr 2006;83:443S-446S. PUBMED | CROSSREF

73. Sikalidis AK. From food for survival to food for personalized optimal health: a historical perspective of how food and nutrition gave rise to nutrigenomics. J Am Coll Nutr 2019;38:84-95. PUBMED | CROSSREF

74. Xu LB, Zhou YF, Yao JL, Sun SJ, Rui Q, Yang XJ, et al. Apolipoprotein A1 polymorphisms and risk of coronary artery disease: a meta-analysis. Arch Med Sci 2017;13:813-819. PUBMED | CROSSREF

75. Abudureyimu S, Abulaiti P, Xing Z, Li H, Liu SS, Li W, et al. The effect of four different single nucleotide polymorphisms on coronary heart disease in a Han Chinese population in Xinjiang region. Research Square. Forthcoming 2021. CROSSREF

76. Morjane I, Charoute H, Elkhattabi L, Saile R, Barakat A. Association of the C. 56C> G *APOA5* gene polymorphism with coronary artery disease: Moroccan case-control study and an updated meta-analysis. Atherosclerosis 2020;315:e189. CROSSREF

77. Al-Tu'ma FJ, Al-Hasnawi NK, Al-Mayali AH. Apolipoprotein A5-1131T>C (RS662799) gene polymorphism as a predictor for coronary artery diseases. World J Pharm Med Res 2019;5:8-12.

78. Hechmi M, Dallali H, Gharbi M, Jmel H, Fassatoui M, Ben Halima Y, et al. Association of rs662799 variant and *APOA5* gene haplotypes with metabolic syndrome and its components: a meta-analysis in North Africa. Biosci Rep 2020;40:BSR20200706. PUBMED | CROSSREF

79. Jacob J, Boczkowska S, Zaluska W, Buraczynska M. Apolipoprotein A5 gene polymorphism (rs662799) and cardiovascular disease in end-stage kidney disease patients. BMC Nephrol 2022;23:307. PUBMED | CROSSREF

80. de Luis DA, Izaola O, Primo D, Aller R. *APOA5* variant rs662799, role in cardiovascular traits and serum adipokine levels in Caucasian obese subjects. Ann Nutr Metab 2021;77:299-306. PUBMED | CROSSREF

81. Morjane I, Charoute H, Ouatou S, Elkhattabi L, Benrahma H, Saile R, et al. Association of c.56C > G (rs3135506) apolipoprotein A5 gene polymorphism with coronary artery disease in moroccan subjects: a case-control study and an updated meta-analysis. Cardiol Res Pract 2020;2020:5981971. PUBMED | CROSSREF

82. Nurmohamed NS, Ditmarsch M, Kastelein JJP. Cholesteryl ester transfer protein inhibitors: from high-density lipoprotein cholesterol to low-density lipoprotein cholesterol lowering agents? Cardiovasc Res 2022;118:2919-2931. PUBMED | CROSSREF

83. Kalantar Z, Eshraghian MR, Sotoudeh G, Djalali M, Mansouri A, Alvandi E, et al. Differences in the interaction between CETP Taq1B polymorphism and dietary fat intake on lipid profile of normolipedemic and dyslipidemic patients with type 2 diabetes mellitus. Clin Nutr 2018;37:270-275. PUBMED | CROSSREF

84. Garcia-Rios A, Alcala-Diaz JF, Gomez-Delgado F, Delgado-Lista J, Marin C, Leon-Acuña A, et al. Beneficial effect of *CETP* gene polymorphism in combination with a Mediterranean diet influencing lipid metabolism in metabolic syndrome patients: CORDIOPREV study. Clin Nutr 2018;37:229-234. PUBMED | CROSSREF

85. Ramezani-Jolfaie N, Aghaei S, Farashahi Yazd E, Moradi A, Mozaffari-Khosravi H, Amiri M, et al. The combined effects of cholesteryl ester transfer protein (*CETP*) TaqIB gene polymorphism and canola, sesame and sesame-canola oils consumption on metabolic response in patients with diabetes and healthy people. J Cardiovasc Thorac Res 2020;12:185-194. PUBMED | CROSSREF

86. Blauw LL, Li-Gao R, Noordam R, de Mutsert R, Trompet S, Berbée JFP, et al. CETP (cholesteryl ester transfer protein) concentration: a genome-wide association study followed by Mendelian randomization on coronary artery disease. Circ Genom Precis Med 2018;11:e002034. PUBMED | CROSSREF

87. Wuni R, Kuhnle GGC, Wynn-Jones AA, Vimaleswaran KS. A nutrigenetic update on *CETP* gene-diet interactions on lipid-related outcomes. Curr Atheroscler Rep 2022;24:119-132. PUBMED | CROSSREF

88. Godonu KG, Momoh JO. Cholesteryl ester transfer protein (*CETP*) I405V (rs5882) polymorphism affects plasma lipid parameters and lipoprotein ratio in hyperlipidemic ischemic stroke patients. Int J Biochem Res Rev 2022;31:11-21. CROSSREF

89. Arikan GD, Isbir S, Yilmaz SG, Isbir T. Characteristics of coronary artery disease patients who have a polymorphism in the cholesterol ester transfer protein (CETP) gene. In Vivo 2019;33:787-792. PUBMED | CROSSREF

90. Annema W, Tietge UJ. Role of hepatic lipase and endothelial lipase in high-density lipoprotein-mediated reverse cholesterol transport. Curr Atheroscler Rep 2011;13:257-265. PUBMED | CROSSREF

91. Perret B, Mabile L, Martinez L, Tercé F, Barbaras R, Collet X. Hepatic lipase: structure/function relationship, synthesis, and regulation. J Lipid Res 2002;43:1163-1169. PUBMED | CROSSREF

92. Ordovas JM, Corella D, Cupples LA, Demissie S, Kelleher A, Coltell O, et al. Polyunsaturated fatty acids modulate the effects of the APOA1 G-A polymorphism on HDL-cholesterol concentrations in a sex-specific manner: the Framingham Study. Am J Clin Nutr 2002;75:38-46. PUBMED | CROSSREF

93. Chatterjee C, Sparks DL. Hepatic lipase, high density lipoproteins, and hypertriglyceridemia. Am J Pathol 2011;178:1429-1433. PUBMED | CROSSREF

94. Zhang C, Lopez-Ridaura R, Rimm EB, Rifai N, Hunter DJ, Hu FB. Interactions between the -514C->T polymorphism of the hepatic lipase gene and lifestyle factors in relation to HDL concentrations among US diabetic men. Am J Clin Nutr 2005;81:1429-1435. PUBMED | CROSSREF

95. Dijk W, Di Filippo M, Kooijman S, van Eenige R, Rimbert A, Caillaud A, et al. Identification of a gain-of-function LIPC variant as a novel cause of familial combined hypocholesterolemia. Circulation 2022;146:724-739. PUBMED | CROSSREF

96. Xu A, Wang W, Jiang X. The roles of *MTRR* and *MTHFR* gene polymorphisms in congenital heart diseases: a meta-analysis. Biosci Rep 2018;38:BSR20181160. PUBMED | CROSSREF

97. Butler S, Young A, Akam EC, Sinha N, Agrawal S, Mastana S. Association of methylenetetrahydrofolate reductase (*MTHFR*) C677T and A1298C polymorphisms with coronary artery disease (CAD) in a North Indian population. Cogent Educ 2018;5:1478477. CROSSREF

98. Shivkar RR, Gawade GC, Padwal MK, Diwan AG, Mahajan SA, Kadam CY. Association of *MTHFR* C677T (rs1801133) and A1298C (rs1801131) polymorphisms with serum homocysteine, folate and vitamin B12 in patients with young coronary artery disease. Indian J Clin Biochem 2022;37:224-231. PUBMED | CROSSREF

99. Amani S, Mirzajani E, Kassaee SM, Mahmoudi M, Mirbolouk F. The association of methylene tetrahydrofolate reductase (*MTHFR*) A1298C gene polymorphism, homocysteine, vitamin B12, and folate with coronary artery disease (CAD) in the north of Iran. Turk Biyokim Derg 2020;45:851-857. CROSSREF

100. Meshkin B, Blum K. Folate nutrigenetics: a convergence of dietary folate metabolism, folic acid supplementation, and folate antagonist pharmacogenetics. Drug Metab Lett 2007;1:55-60. PUBMED | CROSSREF

101. Wu C, Gong Y, Sun A, Zhang Y, Zhang C, Zhang W, et al. The human *MTHFR* rs4846049 polymorphism increases coronary heart disease risk through modifying miRNA binding. Nutr Metab Cardiovasc Dis 2013;23:693-698. PUBMED | CROSSREF

102. Gammelmark A, Nielsen MS, Lundbye-Christensen S, Tjønneland A, Schmidt EB, Overvad K. Common polymorphisms in the 5-lipoxygenase pathway and risk of incident myocardial infarction: a Danish case-cohort study. PLoS One 2016;11:e0167217. PUBMED | CROSSREF

103. Armstrong P, Kelley DS, Newman JW, Staggers FE Sr, Hartiala J, Allayee H, et al. Arachidonate 5-lipoxygenase gene variants affect response to fish oil supplementation by healthy African Americans. J Nutr 2012;142:1417-1428. PUBMED | CROSSREF

104. Allayee H, Baylin A, Hartiala J, Wijesuriya H, Mehrabian M, Lusis AJ, et al. Nutrigenetic association of the 5-lipoxygenase gene with myocardial infarction. Am J Clin Nutr 2008;88:934-940. PUBMED | CROSSREF

105. Tsai AK, Li N, Hanson NQ, Tsai MY, Tang W. Associations of genetic polymorphisms of arachidonate 5-lipoxygenase-activating protein with risk of coronary artery disease in a European-American population. Atherosclerosis 2009;207:487-491. PUBMED | CROSSREF

106. Dwyer JH, Allayee H, Dwyer KM, Fan J, Wu H, Mar R, et al. Arachidonate 5-lipoxygenase promoter genotype, dietary arachidonic acid, and atherosclerosis. N Engl J Med 2004;350:29-37. PUBMED | CROSSREF

107. Tsai MY, Cao J, Steffen BT, Weir NL, Rich SS, Liang S, et al. 5-Lipoxygenase Gene variants are not associated with atherosclerosis or incident coronary heart disease in the multi-ethnic study of atherosclerosis cohort. J Am Heart Assoc 2016;5:e002814. PUBMED | CROSSREF

108. Zhang R, Guo X, Li X, Liu W, Peng Y, Han X, et al. Arachidonate 5-lipoxygenase-activating protein (*ALOX5AP*) gene rs4073259 polymorphism not associated with ischemic stroke in the northeastern Chinese Han population. Clin Neurol Neurosurg 2014;119:64-69. PUBMED | CROSSREF

109. Camacho-Mejorado R, Gómez R, Torres-Sánchez LE, Alhelí Hernández-Tobías E, Noris G, Santana C, et al. *ALOX5*, *LPA*, *MMP9* and *TPO* gene polymorphisms increase atherothrombosis susceptibility in middle-aged Mexicans. R Soc Open Sci 2020;7:190775. PUBMED | CROSSREF

110. Mahmoud R, Kimonis V, Butler MG. Genetics of obesity in humans: a clinical review. Int J Mol Sci 2022;23:11005. PUBMED | CROSSREF

111. Liu C, Mou S, Pan C. The *FTO* gene rs9939609 polymorphism predicts risk of cardiovascular disease: a systematic review and meta-analysis. PLoS One 2013;8:e71901. PUBMED | CROSSREF

112. Franczak A, Kolačkov K, Jawiarczyk-Przybyłowska A, Bolanowski M. Association between *FTO* gene polymorphisms and HDL cholesterol concentration may cause higher risk of cardiovascular disease in patients with acromegaly. Pituitary 2018;21:10-15. PUBMED | CROSSREF

113. Chermon D, Birk R. *FTO* common obesity SNPs interact with actionable environmental factors: physical activity, sugar-sweetened beverages and wine consumption. Nutrients 2022;14:4202. PUBMED | CROSSREF

114. Shahid SU, Shabana , Rehman A, Hasnain S. Role of a common variant of fat mass and obesity associated (*FTO*) gene in obesity and coronary artery disease in subjects from Punjab, Pakistan: a case control study. Lipids Health Dis 2016;15:29. PUBMED | CROSSREF

115. Lappalainen T, Kolehmainen M, Schwab US, Tolppanen AM, Stančáková A, Lindström J, et al. Association of the *FTO* gene variant (rs9939609) with cardiovascular disease in men with abnormal glucose metabolism--the Finnish Diabetes Prevention Study. Nutr Metab Cardiovasc Dis 2011;21:691-698. PUBMED | CROSSREF

116. Äijälä M, Ronkainen J, Huusko T, Malo E, Savolainen ER, Savolainen MJ, et al. The fat mass and obesity-associated (*FTO*) gene variant rs9939609 predicts long-term incidence of cardiovascular disease and related death independent of the traditional risk factors. Ann Med 2015;47:655-663. PUBMED | CROSSREF

117. Mielcarska S, Stopińska K, Poręba M, Szywacz W, Macionga A, Szweda-Gandor N, et al. Influence of the *FTO* polymorphism rs17817449 on the risk of obesity, type 2 diabetes, and cardiovascular diseases in Upper Silesian population—a preliminary, cross-sectional study. Med Res J 2022;7:134-141. CROSSREF

118. Akbari M, Eghtedarian R, Hussen BM, Eslami S, Taheri M, Ghafouri-Fard S. Angiotensin I converting enzyme gene polymorphisms and risk of psychiatric disorders. BMC Psychiatry 2022;22:351. PUBMED | CROSSREF

119. Yousif A, Mir R, Javid J, Barnawi J, Jalal MM, Altayar MA, et al. Clinical utility of amplification refractory mutation system-based PCR and mutation-specific PCR for precise and rapid genotyping of angiotensin-converting enzyme 1 (*ACE1*-rs4646996 D>I) and angiotensin-converting enzyme 2 (*ACE2*-rs4240157T>C) gene variations in coronary artery disease and their strong association with its disease susceptibility and progression. Diagnostics (Basel) 2022;12:1321. PUBMED | CROSSREF

120. Moorthy N, Saligrama Ramegowda K, Jain S, Bharath G, Sinha A, Nanjappa MC, et al. Role of angiotensin-converting enzyme (*ACE*) gene polymorphism and ACE activity in predicting outcome after acute myocardial infarction. Int J Cardiol Heart Vasc 2021;32:100701. PUBMED | CROSSREF

121. Sandeep B, Xiao Z, Gao K, Mao L, Chen J, Ping W, et al. Role and interaction between *ACE1*, *ACE2* and their related genes in cardiovascular disorders. Curr Probl Cardiol 2022;101162: CROSSREF

122. Chiriacò M, Tricò D, Leonetti S, Petrie JR, Balkau B, Højlund K, et al. Female sex and angiotensin-converting enzyme (*ACE*) insertion/deletion polymorphism amplify the effects of adiposity on blood pressure. Hypertension 2022;79:36-46. PUBMED | CROSSREF

123. Zhang Y, Yang T, Zhou W, Huang Y. A meta-analysis on the association of genetic polymorphism of the angiotensin-converting enzyme and coronary artery disease in the Chinese population. Rev Assoc Med Bras 2019;65:923-929. PUBMED | CROSSREF

124. Rashid A, Jafar S, Yaqub RK. Role of peroxisome proliferator-activated receptor (PPAR)-α gene in dyslipidemia. Rawal Med J 2020;45:54-7.

125. Ruscica M, Busnelli M, Runfola E, Corsini A, Sirtori CR. Impact of PPAR-alpha polymorphisms-the case of metabolic disorders and atherosclerosis. Int J Mol Sci 2019;20:4378. PUBMED | CROSSREF

126. Matsunaga T, Naito M, Yin G, Hishida A, Okada R, Kawai S, et al. Associations between peroxisome proliferator-activated receptor γ (PPAR-γ) polymorphisms and serum lipids: Two cross-sectional studies of community-dwelling adults. Gene 2020;762:145019. PUBMED | CROSSREF

127. Kemanci A, Goren T, Uluturk M, Yilmaz A, Sabirli R, Ozen M, et al. The correlation between peroxisome proliferator-activated receptor alpha and gamma polymorphisms and acute coronary syndrome. Cureus 2022;14:e26147. PUBMED | CROSSREF

128. Maciejewska-Skrendo A, Buryta M, Czarny W, Król P, Stastny P, Petr M, et al. The polymorphisms of the peroxisome-proliferator activated receptors' alfa gene modify the aerobic training induced changes of cholesterol and glucose. J Clin Med 2019;8:1043. PUBMED | CROSSREF

129. Belardo D, Michos ED, Blankstein R, Blumenthal RS, Ferdinand KC, Hall K, et al. Practical, evidence-based approaches to nutritional modifications to reduce atherosclerotic cardiovascular disease: an American society for preventive cardiology clinical practice statement. Am J Prev Cardiol 2022;10:100323. PUBMED | CROSSREF

130. Ferraro RA, Fischer NM, Xun H, Michos ED. Nutrition and physical activity recommendations from the United States and European cardiovascular guidelines: a comparative review. Curr Opin Cardiol 2020;35:508-516. PUBMED | CROSSREF

131. Arnett DK, Blumenthal RS, Albert MA, Buroker AB, Goldberger ZD, Hahn EJ, et al. 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation 2019;140:e596-e646. PUBMED | CROSSREF

132. Abaj F, Rafiee M, Koohdani F. Interaction between CETP polymorphism and dietary insulin index and load in relation to cardiovascular risk factors in diabetic adults. Sci Rep 2021;11:15906. PUBMED | CROSSREF

133. Hosseini-Esfahani F, Esfandiar Z, Mirmiran P, Daneshpour MS, Ghanbarian A, Azizi F. The interaction of cholesteryl ester transfer protein gene variations and diet on changes in serum lipid profiles. Eur J Clin Nutr 2019;73:1291-1298. PUBMED | CROSSREF

134. Minieri M, Di Nardo P. Nutrients: the environmental regulation of cardiovascular gene expression. Genes Nutr 2007;2:163-168. PUBMED | CROSSREF

135. Jinnette R, Narita A, Manning B, McNaughton SA, Mathers JC, Livingstone KM. Does personalized nutrition advice improve dietary intake in healthy adults? A systematic review of randomized controlled trials. Adv Nutr 2021;12:657-669. PUBMED | CROSSREF

136. Zhang X, Qi Q, Bray GA, Hu FB, Sacks FM, Qi L. APOA5 genotype modulates 2-y changes in lipid profile in response to weight-loss diet intervention: the Pounds Lost Trial. Am J Clin Nutr 2012;96:917-922. PUBMED | CROSSREF

137. de Luis D, Izaola O, Primo D, Aller R. Role of rs670 variant of *APOA1* gene on metabolic response after a high fat vs. a low fat hypocaloric diets in obese human subjects. J Diabetes Complications 2019;33:249-254. PUBMED | CROSSREF

138. Xu M, Ng SS, Bray GA, Ryan DH, Sacks FM, Ning G, et al. Dietary fat intake modifies the effect of a common variant in the *LIPC* gene on changes in serum lipid concentrations during a long-term weight-loss intervention trial. J Nutr 2015;145:1289-1294. PUBMED | CROSSREF

139. Smith CE, Van Rompay MI, Mattei J, Garcia JF, Garcia-Bailo B, Lichtenstein AH, et al. Dietary fat modulation of hepatic lipase variant -514 C/T for lipids: a crossover randomized dietary intervention trial in Caribbean Hispanics. Physiol Genomics 2017;49:592-600. PUBMED | CROSSREF

140. Qi Q, Durst R, Schwarzfuchs D, Leitersdorf E, Shpitzen S, Li Y, et al. CETP genotype and changes in lipid levels in response to weight-loss diet intervention in the POUNDS LOST and DIRECT randomized trials. J Lipid Res 2015;56:713-721. PUBMED | CROSSREF

141. Schüler R, Osterhoff MA, Frahnow T, Seltmann AC, Busjahn A, Kabisch S, et al. High-saturated-fat diet increases circulating angiotensin-converting enzyme, which is enhanced by the rs4343 polymorphism defining persons at risk of nutrient-dependent increases of blood pressure. J Am Heart Assoc 2017;6:e004465. PUBMED | CROSSREF

142. Corella D, Carrasco P, Sorlí JV, Estruch R, Rico-Sanz J, Martínez-González MÁ, et al. Mediterranean diet reduces the adverse effect of the TCF7L2-rs7903146 polymorphism on cardiovascular risk factors and stroke incidence: a randomized controlled trial in a high-cardiovascular-risk population. Diabetes Care 2013;36:3803-3811. PUBMED | CROSSREF

143. Ortega-Azorín C, Sorlí JV, Estruch R, Asensio EM, Coltell O, González JI, et al. Amino acid change in the carbohydrate response element binding protein is associated with lower triglycerides and myocardial infarction incidence depending on level of adherence to the Mediterranean diet in the PREDIMED trial. Circ Cardiovasc Genet 2014;7:49-58. PUBMED | CROSSREF

144. Corella D, Sorlí JV, Estruch R, Coltell O, Ortega-Azorín C, Portolés O, et al. MicroRNA-410 regulated lipoprotein lipase variant rs13702 is associated with stroke incidence and modulated by diet in the randomized controlled PREDIMED trial. Am J Clin Nutr 2014;100:719-731. PUBMED | CROSSREF

145. de Luis DA, Izaola O, Primo D, Aller R. Role of rs670 variant of *APOA1* gene on lipid profile, insulin resistance and adipokine levels in obese subjects after weight loss with a dietary intervention. Diabetes Res Clin Pract 2018;142:139-145. PUBMED | CROSSREF

146. Gomez-Delgado F, Alcala-Diaz JF, Garcia-Rios A, Delgado-Lista J, Ortiz-Morales A, Rangel-Zuñiga O, et al. Polymorphism at the TNF-alpha gene interacts with Mediterranean diet to influence triglyceride metabolism and inflammation status in metabolic syndrome patients: from the CORDIOPREV clinical trial. Mol Nutr Food Res 2014;58:1519-1527. PUBMED | CROSSREF

147. Fallaize R, Celis-Morales C, Macready AL, Marsaux CF, Forster H, O'Donovan C, et al. The effect of the apolipoprotein E genotype on response to personalized dietary advice intervention: findings from the Food4Me randomized controlled trial. Am J Clin Nutr 2016;104:827-836. PUBMED | CROSSREF

148. Shatwan IM, Weech M, Jackson KG, Lovegrove JA, Vimaleswaran KS. Apolipoprotein E gene polymorphism modifies fasting total cholesterol concentrations in response to replacement of dietary saturated with monounsaturated fatty acids in adults at moderate cardiovascular disease risk. Lipids Health Dis 2017;16:222. PUBMED | CROSSREF

149. Ordovas JM, Corella D, Demissie S, Cupples LA, Couture P, Coltell O, et al. Dietary fat intake determines the effect of a common polymorphism in the hepatic lipase gene promoter on high-density lipoprotein metabolism: evidence of a strong dose effect in this gene-nutrient interaction in the Framingham Study. Circulation 2002;106:2315-2321. PUBMED | CROSSREF

150. Fitó M, Melander O, Martínez JA, Toledo E, Carpéné C, Corella D. Advances in integrating traditional and omic biomarkers when analyzing the effects of the Mediterranean diet intervention in cardiovascular prevention. Int J Mol Sci 2016;17:1469. PUBMED | CROSSREF

151. Liberale L, Montecucco F, Tardif JC, Libby P, Camici GG. Inflamm-ageing: the role of inflammation in age-dependent cardiovascular disease. Eur Heart J 2020;41:2974-2982. PUBMED | CROSSREF

152. Sorriento D, Iaccarino G. Inflammation and cardiovascular diseases: the most recent findings. Int J Mol Sci 2019;20:3879. PUBMED | CROSSREF

153. Hidalgo-Moyano C, Rangel-Zuñiga OA, Gomez-Delgado F, Alcala-Diaz JF, Rodriguez-Cantalejo F, Yubero-Serrano EM, et al. Diet and *SIRT1* genotype interact to modulate aging-related processes in patients with coronary heart disease: from the CORDIOPREV study. Nutrients 2022;14:3789. PUBMED | CROSSREF

154. King A, Saifi S, Smith J, Pilic L, Graham CA, Da Silva Anastacio V, et al. Does personalised nutrition advice based on apolipoprotein E and methylenetetrahydrofolate reductase genotype affect dietary behaviour? Nutr Health 2022;28:467-476. PUBMED | CROSSREF

155. MacKay DS, Eck PK, Gebauer SK, Baer DJ, Jones PJ. *CYP7A1-rs3808607* and *APOE* isoform associate with LDL cholesterol lowering after plant sterol consumption in a randomized clinical trial. Am J Clin Nutr 2015;102:951-957. PUBMED | CROSSREF

156. Chang SL, Nfor ON, Ho CC, Lee KJ, Lu WY, Lung CC, et al. Combination of exercise and vegetarian diet: relationship with high density-lipoprotein cholesterol in Taiwanese adults based on *MTHFR* rs1801133 polymorphism. Nutrients 2020;12:1564. PUBMED | CROSSREF