



Nutrigenomic Interactions between Omega-3 Fatty Acids and Inflammatory Gene Expression in Metabolic Syndrome: A Review

Sani Shuaibu Kafin Hausa^{1,2}, Mustapha Sabo Abdullahi¹, Amina Bala Saad^{1,4}, Nura Baffa Musa³, Amir Auwal Bello³ & Abdullahi Hussaini⁵

¹Department of Biology, Khadija University Majia, Taura-Jigawa State

²Department of Microbiology and Biotechnology, Federal University Dutse, Jigawa State

³Department of Food Science and Technology, Kano University of Science and Technology Wudil.

⁴Department of Plant Science and Biotechnology, Federal University Dutsin-ma, Katsina State.

⁵Department of Science Laboratory Technology, Binyaminu Usman Polytechnic Hadejia, Jigawa State.

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*Corresponding Author: Sani Shuaibu Kafin Hausa

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Abstract

Review Article

Nutrigenomics investigates how nutrients interact with genes to affect health outcomes. Among these nutrients, omega-3 fatty acids, especially EPA and DHA, have been identified as significant dietary elements that can modulate gene expression linked to inflammation. Since inflammation plays a crucial role in metabolic syndrome (MetS), understanding the molecular and nutrigenomic mechanisms by which omega-3s influence inflammatory gene expression is essential. This review examines recent developments in the role of omega-3 fatty acids in regulating inflammatory pathways related to MetS, drawing on evidence from clinical trials, molecular studies, and personalized nutrition approaches to demonstrate the potential for specific nutritional interventions.

Keywords: Nutrigenomics, Omega-3 Fatty Acids, Inflammatory Genes, Metabolic Syndrome, Gene Expression, Personalized Nutrition, EPA, DHA.

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1. Introduction

Nutrigenomics, a subset of nutritional genomics, studies how diet affects the genome and influences human health. This field presents promising strategies for personalized nutrition, especially for chronic conditions like metabolic syndrome (MetS), where individuals' dietary responses can vary widely (Calder, 2020). MetS consists of a series of interconnected metabolic issues, including central obesity, insulin resistance, abnormal lipid levels, and high blood pressure, which significantly increase the risk of cardiovascular disease and type 2 diabetes. Recent

studies suggest that low-grade chronic inflammation is a key factor in the development of MetS (de Mello *et al.*, 2018). Omega-3 polyunsaturated fatty acids (PUFAs), notably EPA and DHA, have been extensively researched for their anti-inflammatory effects, impacting gene expression through various transcriptional and post-transcriptional pathways. Their capacity to regulate gene networks related to inflammation has made them a focus in nutrigenomic studies. Investigating the relationship between omega-3 intake and gene expression could lead to innovative dietary strategies for the prevention and management of MetS (García-Rodríguez *et al.*,



2020).

The inclusion of omega-3 fatty acids in the diet is linked to reduced expression of several pro-inflammatory genes, such as TNF- α , IL-6, and NF- κ B, through both direct alterations in transcription factors and indirect effects via lipid signaling pathways. Recent advancements in high-throughput gene expression technologies have deepened our understanding of these intricate relationships (Muhlhausler *et al.*, 2017).

This review aims to consolidate existing knowledge regarding the nutrigenomic effects of omega-3 fatty acids on inflammatory gene expression in the context of MetS, focusing on molecular mechanisms, clinical findings, and personalized nutrition implications while referencing literature published in the past eight years (Minihane *et al.*, 2016).

2. Molecular Mechanisms of Omega-3 Fatty Acids in Gene Regulation

Omega-3 fatty acids impact gene expression by acting as signaling molecules and ligands for transcription factors. EPA and DHA activate nuclear receptors like peroxisome proliferator-activated receptors (PPARs), particularly PPAR- γ , which is crucial for lipid metabolism, insulin sensitivity, and inflammation (Calder, 2020). When PPAR- γ is activated, it pairs with the retinoid X receptor (RXR) to bind to specific response elements in the promoter regions of target genes, leading to their activation or repression (de Mello *et al.*, 2018).

Additionally, omega-3 fatty acids impede the NF- κ B pathway, a key regulator of inflammatory processes. Normally, NF- κ B is kept inactive in the cytoplasm by I κ B proteins. When stimulated by pro-inflammatory signals, I κ B degrades, allowing NF- κ B to move to the nucleus and trigger transcription of pro-inflammatory genes like TNF- α and IL-6. Omega-3 fatty acids can reduce this signaling cascade, thereby lowering inflammation.

Epigenetic changes also play a role in how omega-3s regulate gene expression. They can modify DNA methylation and histone patterns in important metabolic tissues, leading to long-lasting alterations in gene transcription. For example, DHA has been shown to influence histone acetylation, impacting the

transcription of inflammatory genes (García-Rodríguez *et al.*, 2020).

Furthermore, omega-3s promote the synthesis of specialized pro-resolving mediators (SPMs) like resolvins and protectins, which actively help resolve inflammation and can modulate gene expression through interactions with G-protein coupled receptors and associated signaling pathways (Calder, 2020). The combined effects of transcriptional, epigenetic, and signaling mechanisms highlight the significant nutrigenomic impact of omega-3 fatty acids on inflammation.

3. Nutrigenomic Evidence from Clinical and Experimental Studies

A variety of clinical trials and experimental research have confirmed the nutrigenomic effects of omega-3 fatty acids on inflammatory gene expression in the context of MetS. For example, in a randomized controlled trial conducted by de Mello *et al.* (2018), overweight participants with MetS characteristics who received 2 g/day of EPA/DHA for 12 weeks exhibited significant decreases in IL-6 and TNF- α mRNA levels in peripheral blood mononuclear cells, reinforcing the anti-inflammatory effects of omega-3s.

Similarly, Romagnolo and Selmin (2017) investigated gene expression in humans following omega-3-rich diets, finding substantial changes in over 100 genes related to lipid metabolism, glucose regulation, and inflammatory responses. These results indicate that omega-3s exert a broad influence over metabolic and immune pathways, showcasing their potential in managing MetS.

Animal studies further validate these findings. Rodent models supplemented with EPA and DHA demonstrated a reduction in hepatic inflammatory cytokine production and improved insulin sensitivity, with observable effects on various metabolic regulators at both the mRNA and protein levels (Romagnolo and Selmin, 2017). Such models are crucial for uncovering the mechanisms and interactions between genes and nutrients in living organisms.

Research has also examined how genetic variations affect responses to omega-3 intake. Variants in genes



like FADS1 and TLR4 may influence the efficacy of omega-3 supplementation, suggesting that individuals with specific genetic profiles could experience more significant anti-inflammatory effects, underscoring the importance of incorporating genetic assessment into dietary strategies.

4. Implications for Personalized Nutrition and Public Health

Implementing nutrigenomics in clinical nutrition offers significant potential for the prevention and management of metabolic syndrome (Romagnolo and Selmin, 2017). Tailoring nutrition plans based on genetic profiles allows interventions to be personalized according to how individuals' genes interact with their diet, particularly benefiting those with high inflammatory gene expression from omega-3 diets (Minihane *et al.*, 2016).

Additionally, insights from nutrigenomics can enhance risk assessment and early intervention approaches. By identifying individuals prone to inflammation-related MetS, targeted omega-3 supplementation can serve as a proactive strategy to mitigate health issues associated with chronic diseases and improve overall quality of life (García-Rodríguez *et al.*, 2020).

From a public health standpoint, incorporating nutrigenomic insights into dietary guidelines may refine recommendations at the population level (Minihane *et al.*, 2016). For instance, encouraging increased omega-3 consumption through fortified foods or supplements could be highlighted for groups with higher MetS risks. Educational efforts could also promote awareness about the benefits of omega-3s and their relationship to genetics (Tindall *et al.*, 2022).

Conclusion

Future research should focus on establishing reliable biomarkers for nutrient-gene interactions and validating these across diverse populations. Collaboration among geneticists, nutritionists, and

clinicians is vital for applying nutrigenomic findings effectively. Ultimately, harnessing the nutrigenomic potential of omega-3 fatty acids could transform dietary strategies for managing inflammation and metabolic disorders.

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