Review

AN OVERVIEW OF THE RELATIONSHIP BETWEEN DIETARY BEHAVIOR AND LIFESTYLE TO HEALTH AT MOLECULAR BIOLOGY MECHANISM

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ABSTRACT

Following the green revolutions, the industrial revolution, and the fourth industrial wave, the quantity of food, goods, and products that serve human life has reached unprecedented levels. Advancements in agriculture productivity, production, and processing technologies, as well as smart supply chain control, have contributed to the "surplus crisis" of food in most countries, including Vietnam. The majority of the world's population consumes diets with excessive levels of fat, sugar, salt, and a lack of fiber. These unhealthy eating habits are known to be the main causes of chronic diseases, acting as silent killers of the health and lifespan of contemporary human society. Fortunately, a new trend of nutritious diets rich in fiber, positive thinking habits, exercise, and a harmonious lifestyle has been discovered as a "reform pill" for humans.

This article presents a synthesis and update of relevant research achievements, with the ambition to positively adjust unscientific eating habits and change negative thinking and behavior to improve the health and lifespan of human society.

Keywords: *behavioral science, disease, eating behavior, exercise, epigenetic, nutrigenomics, metabolism*

I. INTRODUCTION

A lifestyle is the sum of motives, needs, and desires and is influenced by factors like culture, family, and social relationships [1]. Nutritional behavior comprises all planned, spontaneous, or habitual actions of individuals or social groups to obtain, prepare, consume food, and store or dispose of it. The behavior not only pertains to its influencing factors but also affects health, the environment, society, and the economy [2]. A healthy person, as defined by the World Health Organization, is someone who is completely at ease physically, mentally, and socially [3].

Vietnamese's lifestyle, nutritional behavior, and culinary culture have had a significant impact on their health, physique, and lifespan of them due to their thousand-year-old process and self-sufficient production mechanisms [4]. The local supply chains were short, and most Vietnamese people's basic diet only met the minimum needs to be full. Rice, corn, cassava, and vegetables were the primary sources of energy. Nutrient-rich products from animals and plants were limited due to low yields of crops and livestock, poor soil, and weak technology [5]. This has led to the

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Submitted: March 26, 2023
Revised: April 25, 2023
Accepted: April 25, 2023
Published online: April 28, 2023

limited physique and health of Vietnamese people over many generations. In 1938, two French experts, Huard and Bigot, measured the height and weight of 4,545 Vietnamese adults living in the rural areas of the Hong River in northern Vietnam. The results showed that the average height of adult males was 160 cm and that of females was 150 cm. The average weight of adult males was 47.3 kg [6]. Forty years later, the initial study (1938−1976), as well as subsequent research conducted by Nguyen Cong Khan and colleagues, revealed that there was no significant change in the height of both genders, and this condition may be related to the difficult living conditions during the prolonged period of war [7].

In recent decades, globalized knowledge and farming practices have led to a synchronized increase in the quantity and quality of food products, meeting the majority's taste needs. Animal-sourced and beverage products, such as meat, fish, butter, eggs, milk, beer, soft drinks, fast food, and pre-packaged food, have completely transformed the Vietnamese lifestyle, nutritional behavior, and health in both positive and negative ways. Though it has improved and enhanced health and physical status, it has also caused negative

Currently, the trend of chronic diseases is increasing globally and particularly in Vietnam each year. These diseases are not infectious and have prolonged and slow progression. The causes of these diseases include various factors such as genetics, physiology, behavior, and the quality of the living environment. According to the World Health Organization (WHO) in 2019, non-communicable diseases are the leading cause of death worldwide, accounting for 71% of total deaths per year. According to data from the World Bank's "Cause of death, by non-communicable diseases (% of total) - Least developed countries: UN classification" in 2019, the mortality rates in the United States (88.14%), Germany (90.6%), Vietnam (81.37%), Laos (65.34%), and India (65.93%) [8]. The top four leading killers with the highest number of deaths are cardiovascular diseases (17.9 million deaths per year), cancer (9.0 million), respiratory diseases (3.9 million), and diabetes (1.6 million) [9]. Among them, the habits of consuming high amounts of salt, sugar, fat, and smoking in adults are the main causes [10].

Epigenetics is a field of study focused on understanding how behavior and environmental factors can cause changes in gene regulation, including processes such as gene methylation, histone modification (acetylation), and microRNA (miRNA) regulation [11]. Disorders of metabolism such as obesity, glucose intolerance, insulin resistance, hypertension, and dyslipidemia are associated with unhealthy dietary and lifestyle behaviors. They are linked to an increased risk of chronic diseases such as type 2 diabetes, cardiovascular disease, and certain cancers [12,13]. The impact of epigenetic changes is not only a concern for public health globally but also for the health of the Vietnamese community. Unhealthy dietary and lifestyle behaviors not only affect the health of adults but also affect the development and increase the risk of metabolic disorders in the offspring during pregnancy [14].

Gene methylation involves the addition of a methyl (CH_3) group to cytosine (C) in DNA by the enzyme DNA methyltransferases (DNMT), which prevents transcription factors from binding to DNA, resulting in a disruption of the transcription process. In contrast, the demethylation process is catalyzed by ten-eleven translocation methylcytosine dioxygenases (TET), which allows transcription factors to bind to DNA and activate the transcription process [13,15].

DNA is tightly wrapped around histone proteins in chromatin, preventing transcription factors from accessing the gene. Acetylation by the enzymes histone acetyltransferase (HAT), histone deacetylases (HDAC), and NAD-dependent deacetylase sirtuin (SIRT) can affect transcription factors by modifying histone acetylation. HAT participates in histone acetylation, which helps to unwind the chromatin structure, and activate gene transcription. HDAC and SIRT participate in histone deacetylation, which leads to chromatin condensation and inhibition of gene transcription [13,16].

II. METHODS

We conducted a thorough review of existing literature on the relationship between dietary behavior and health at the molecular biology level. Relevant scientific literature was comprehensively examined and analyzed using keywords such as Behavioral science, disease, eating behavior, exercise, epigenetics, nutrigenomics, and metabolism. Researchers searched systematically using different reputable databases such as Google Scholar, Springer, PubMed, and ScienceDirect. The selected studies and publications included full research articles, short communications, and review articles presenting results from experimental studies, clinical trials, and survey data. The publications selected were published between 2008 and 2022. Based on the title screening of 212 articles, we narrowed it down to 17 related publications (excluding those that did not have representative samples or were focused on Vietnamese communities living abroad). Further examination of abstracts and full texts led to the selection of 3 relevant articles. We also searched for relevant reports in the libraries of various organizations, including the World Health Organization, the World Bank, research institutes, universities, and non-governmental organizations.

III. UPDATE ON MOLECULAR BIOLOGICAL CHANGES BETWEEN OBESITY AND DIETARY HABITS, PHYSICAL ACTIVITY

3.1. Adipose tissue and obesity

In the human adipose tissue, three types of adipocytes exist white adipose tissue, brown adipose tissue, and beige adipose tissue. These adipocytes differ fundamentally in their triglyceride and mitochondria content within the cells (Figure 1).

White adipose tissue has the highest concentration of triglycerides, followed by beige adipose tissue and brown adipose tissue. This results in white adipose tissue having a greater energy storage capacity compared to the other two types of adipose tissue. Additionally, white adipose tissue has the least amount of mitochondria, beige adipose tissue has more and brown adipose tissue has the highest amount of mitochondria. As a result, brown adipose tissue tends to expend more energy in comparison to the other two types of adipose tissue [17]. Accumulation of white adipose tissue in excessive amounts leads to weight gain, and can ultimately lead to obesity.

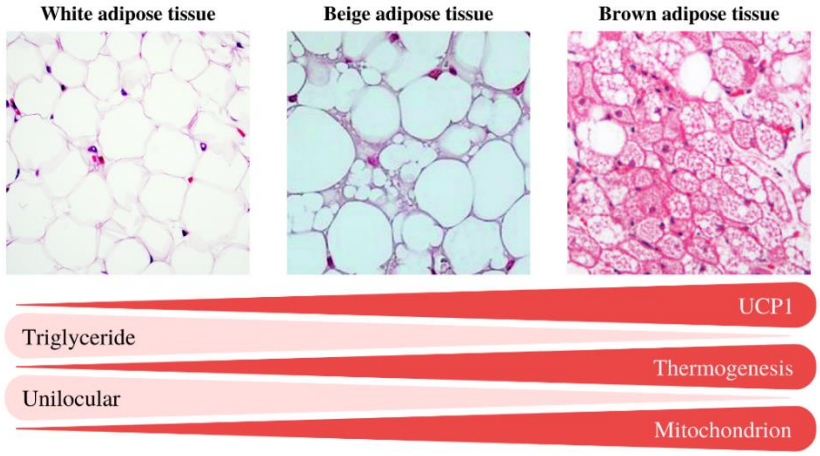

Figure 1. *Comparison of the three types of adipose tissue, white adipose tissue, beige adipose tissue, and brown adipose tissue [17]*

3.2. The harmful effects of a high-fructose and fat diet

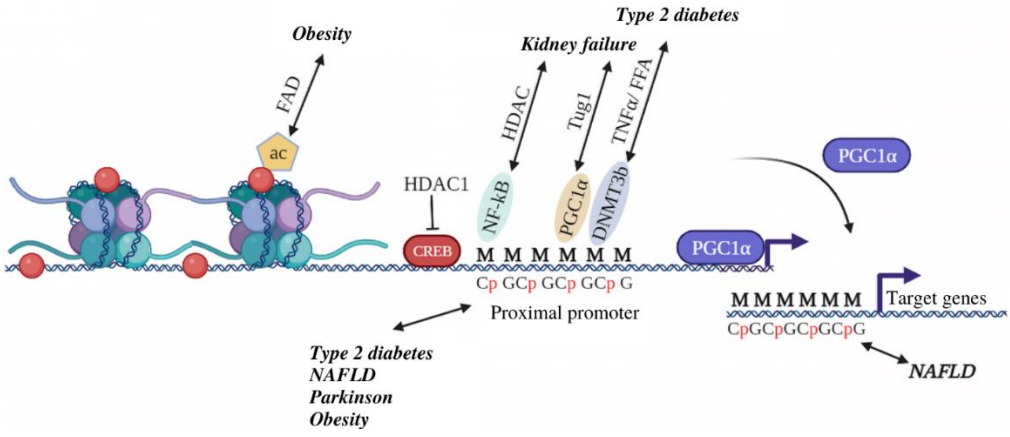

Figure 2. *The relationship between promoter methylation of the PGC1α gene and type 2 diabetes, non-alcoholic fatty liver disease, Parkinson's disease, and obesity [18]*

The formation of brown fat is mediated by genes including UCP1, PRDM16, FNDC5, CD137, and genes involved in mitochondrial biogenesis such as NRF1, TFAM, PGC1α, PPARα, and citrate synthase. Depending on environmental conditions and lifestyle choices, the formation of the three types of adipose

tissue can vary between individuals. PGC1α is a mitochondrial biogenesis gene that participates in the process of beta-oxidation, which converts white fat into brown fat. This conversion process helps to expend energy and burn excess fat. A high-fat diet has been found to cause methylation of the promoter of the PGC1α gene in pregnant C57BL/6 mice, leading to inhibition of the transcriptional process and a decrease in mitochondrial biogenesis. This results in an increase in the formation and accumulation of white fat in the body, which in turn increases the risk of overweight, obesity, insulin resistance, non-alcoholic fatty liver disease, and Parkinson's disease (Figure 2) [18,19]. A study by S.C. Jacobsen et al. (2012) showed that a high-fat diet in males increased methylation of the PGC-1α gene in bone cells, leading to an increased risk of metabolic disorders, including type 2 diabetes [20].

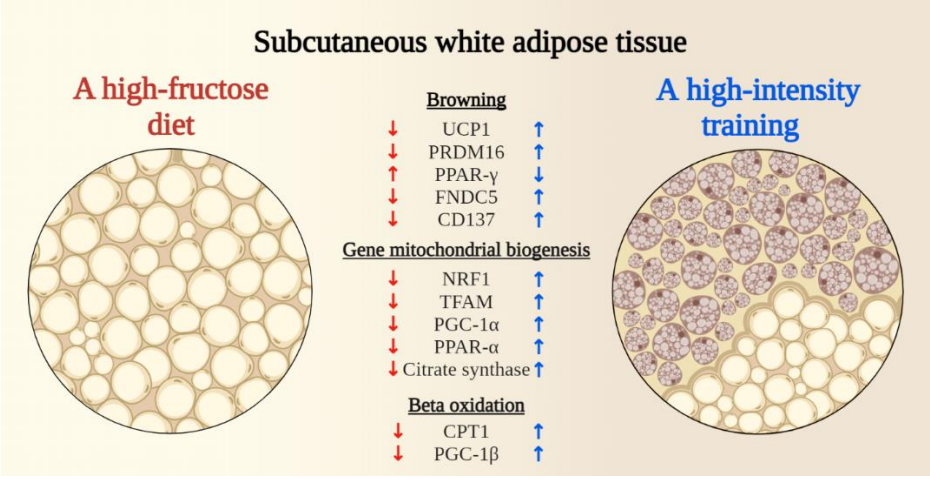

Figure 3. *The relationship between fructose consumption and high-intensity interval training [21]*

Multiple studies have also demonstrated that high-intensity exercise can increase the ability to demethylate gene promoters and improve the expression of genes including PGC1α, PDK4, TFAM, CS, and MEF2A, which can help to prevent the risk of overweight, obesity, and insulin resistance. Furthermore, a high fructose diet can reduce the expression of brown fat genes, increase the formation of subcutaneous white adipose tissue, and contribute to weight gain and obesity (Figure 3) [19,21].

3.3. The relationship between smoking and a diet rich in fructose and fat for some other diseases

SIRT1, a NAD-dependent deacetylase, is an enzyme that functions in the deacetylation of histone tail molecules. This process supports gene packaging, represses gene transcription, and modulates the acetylation status of various protein molecules such as FOXO1, NF-kB, CREB, c-Myc, PPARγ to regulate the internal environment of the organism. SIRT1 is involved in the deacetylation of the p65 subunit of NF-kB, leading to the inactivation of NF-kB, and removes acetyl groups from the histone tail at position H4K16, which facilitates chromatin packaging and transcriptional repression of cytokine genes [22,23].

The act of smoking induces the production of free radicals, which leads to the inhibition of the SIRT1, thereby reducing its ability to deacetylate histone tails at the H4K16 position of chromatin and the p65 subunit of the transcription factor NF-kB. As a result, histone acetylation occurs, leading to chromatin relaxation and the activation of the NF-kB signaling pathway, which promotes the transcription of inflammatory genes such as TNF-α, IL-6, and IL-1β [22,24]. This, in turn, leads to an imbalance between pro-inflammatory cytokines in Th17 cells and anti-inflammatory cytokines in T reg cells, altering the IgG4/ IgE antibody ratio in B lymphocytes and ultimately increasing the risk of developing chronic diseases, allergies, and asthma [25]. Furthermore, smoking is associated with neurodegeneration and cerebrovascular diseases [26]. Additionally, consuming a diet that is high in fructose and fat can induce intestinal inflammation, which is caused by the presence of harmful bacteria such as Proteobacteria and Bacteroides that secrete lipopolysaccharides [27].

An unhealthy lifestyle, including smoking and a diet high in fructose and fat, promotes inflammatory reactions that increase the risk of chronic diseases, asthma, and allergies [25]. Inflammatory cytokines also damage adipose tissue cells, reducing the expression of adiponectin, an adipokine related to regulating glucose uptake and fatty acid breakdown, leading to the accelerated formation of triglycerides in white fat cells, causing weight gain and obesity (Figure 4) [27].

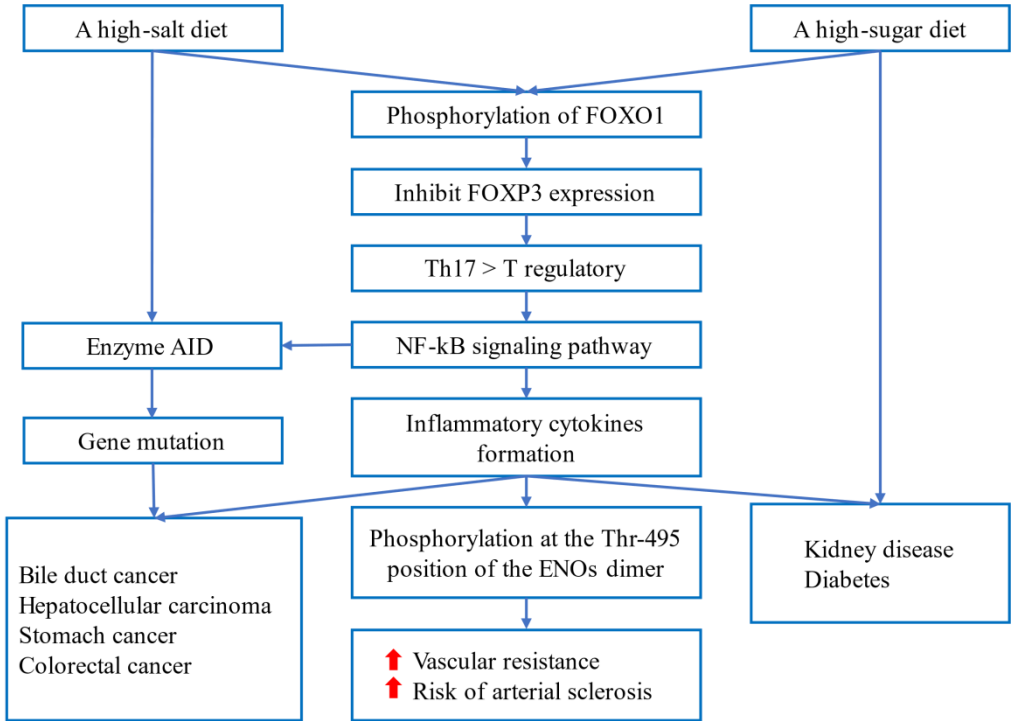

Figure 4. *The relationship between a high sugar-salt diet and many diseases originating from the phosphorylation of FOXO1.*

3.4. The relationship between a high-sugar, high-salt diet and certain diseases

A high-salt diet directly causes phosphorylation at the Thr24, Ser256, and Ser319 positions, which inhibits the activity of the transcription factor FOXO1 protein, reducing the expression of FOXP3 mRNA and leading to Treg differentiation. This leads to an imbalance between the Th17 and Treg immune cell systems, resulting in an imbalance between pro-inflammatory cytokines and anti-inflammatory cytokines [28]. A high-salt diet is closely correlated with the activation of pro-inflammatory signaling molecules such as NF-kB [29]. NF-kB participates in the transcription process of the formation of the AID enzyme, which changes the nucleotide sequence between C: G to U: G, causing gene mutations and leading to the development of various cancers, including gallbladder cancer, hepatocellular carcinoma, gastric cancer, colorectal cancer, and diabetic kidney disease [30,31]. In addition to a high-salt diet, a high-sugar diet also contributes to the phosphorylation of FOXO1, damaging kidney function and causing diabetic kidney disease [32,33]. The promotion of pro-inflammatory cytokines (IL-17) due to a high-salt diet also contributes to the phosphorylation of the eNOS dimer at the Thr-495 position, leading to a decrease in nitric oxide, an increase in vascular resistance, and the formation of hypertension, atherosclerosis, tumor growth, heart and brain damage, and stroke (Figure 5) [34].

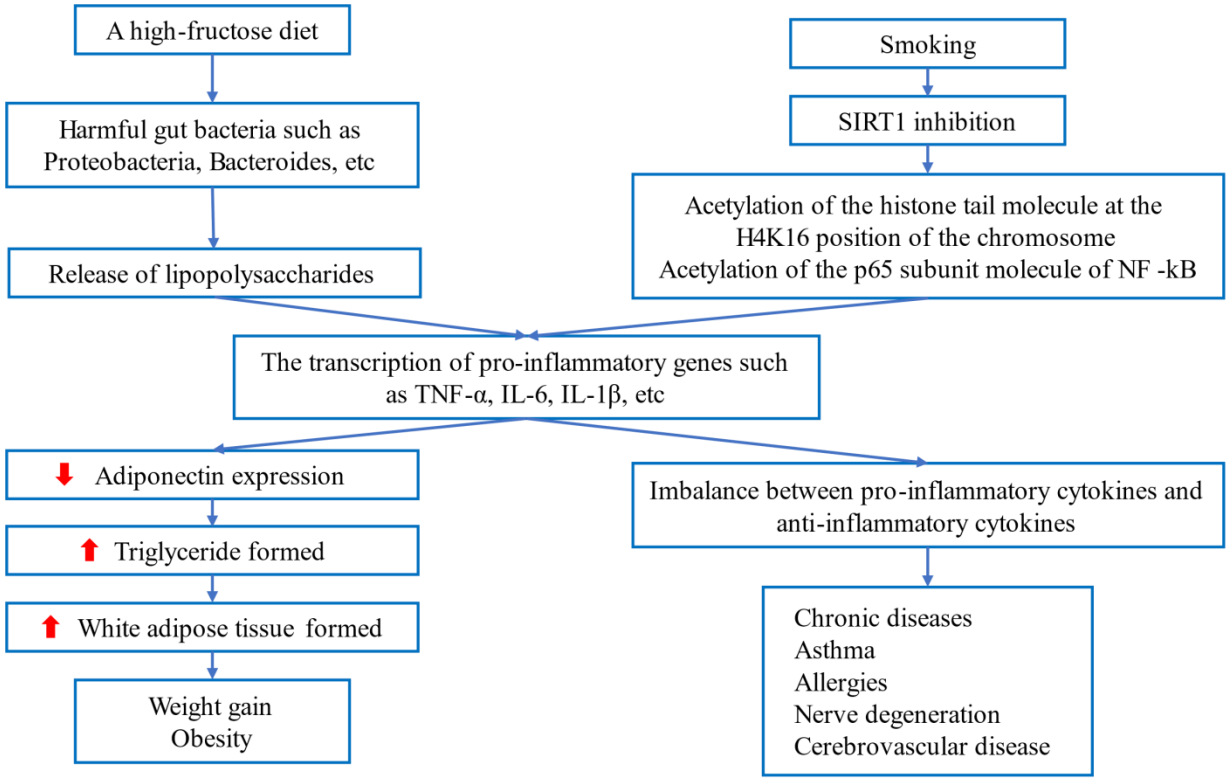

Figure 5. *The relationship between smoking and a diet high in fructose and fat for obesity.*

In summary, through the synthesis of various literature, the relationship between high fructose, fat, sugar, salt consumption, and smoking behavior has been established as having an impact on health through genetic, epigenetic, immune, and metabolic pathways. The "three-legged stool" relationship between genetic, epigenetic, immune, and metabolic pathways plays a critical role in the expression of genes involved in cytokine production, inflammation, and lipogenesis such as acetyl-CoA carboxylase 1, fatty acid synthase, and acyl-CoA desaturase, increasing the risk of non-communicable diseases. The interplay and coherence between dietary and lifestyle behavior through this three-legged stool system will contribute to guiding behavioral adjustment-based methods for the treatment of non-communicable diseases.

IV. A FIBER-RICH DIET PREVENTS MANY DISEASES

4.1. Adipose tissue and obesity

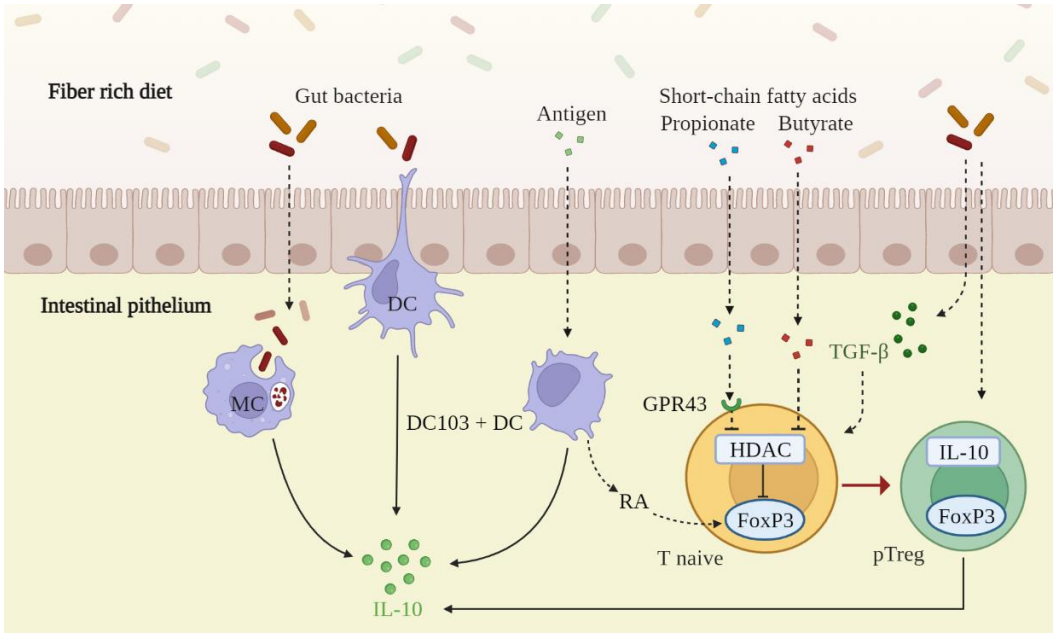

Figure 6. *HDAC inhibits FOXP3. Short-chain fatty acid chains inhibit HDAC through histone acetylation to open the unwound gene, activate the transcription process of FOXP3 to differentiate naive T cells into regulatory T cells, releasing anti-inflammatory cytokines IL-10 [39].*

The fibroblast growth factor 21 (FGF21) hormone is a versatile hormone that helps balance the internal environment, along with PGC1α that converts white fat tissue into beige and brown fat, while also preventing inflammatory reactions that cause many diseases, including pancreatic cancer [35]. Obesity, type 2 diabetes, and a high-fat diet are causes that increase the methylation of the FGF21 gene promoter. They inhibit the transcription process and expression of the FGF21 gene, leading to an increase in the formation and accumulation of white fat tissue, and worsening inflammation leading to pancreatic cancer and low bone joint inflammation [36,37]. Short-chain fatty acids including

butyric acid and α-lipoic acid are products of the fermentation process of gut bacteria due to a fiber-rich diet. Under the action of the acyl-CoA synthetases enzyme group, short-chain fatty acids are converted to acyl-CoA fatty acids, and then under the action of the beta-oxidation process into acetyl-CoA [38]. Acetyl-CoA under the action of the HAT and HDAC enzymes affects the transcription factor of the gene. HAT participates in the acetylation of histones, helping to open the unwound gene, activating the transcription process of the gene (ON), and forming the FOXP3 protein. FOXP3 participates in the transcription and translation process to secrete anti-inflammatory cytokines, typically IL-10, to inhibit Th2 secretion of inflammatory cytokines. In contrast, HDAC participates in the deacetylation of histones, helping to package the unwound gene, inhibiting the transcription process of the gene (OFF), and inhibiting the differentiation process of naive T cells into regulatory T cells (Figure 6) [39,40].

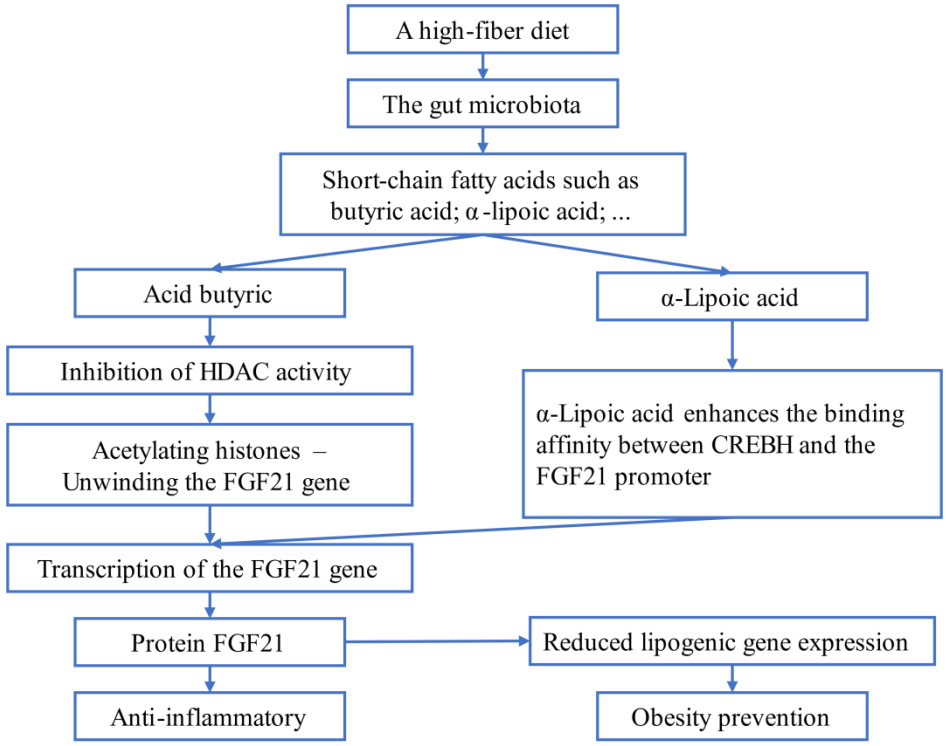

Figure 7. *Mechanism of the benefits of a fiber-rich diet in increasing the expression of the FGF21 gene to prevent inflammation and obesity.*

Butyric acid inhibits the activity of the HDAC enzyme, prevents histone deacetylation, and increases histone acetylation to prepare the FGF21 gene for transcription. At the same time, α-lipoic acid increases the binding between CREBH and the FGF21 promoter for the transcription process of the gene to form the FGF21 hormone. A diet rich in α-lipoic acid helps to inhibit and reduce the expression of lipogenic genes such as acetyl-CoA carboxylase 1, fatty acid synthase, acyl-CoA desaturase 1, elongation of very long chain fatty acids protein 6, and glycerol-3-phosphate acyltransferase 1 (Figure 7) [41].

V. PHYSICAL ACTIVITIES

5.1. History of collective exercise

The practice of collective exercise has been an integral part of human physical activity for a significant period, dating back to 2.5 million years BC, and intertwined with human survival throughout history. Our prehistoric ancestors were adept at endurance activities, utilizing stone tools for activities such as gathering, hunting, and fleeing to safeguard their lives. Moreover, our ancestors also experienced a momentous migration event from Africa to the Americas around 12,000 BC [42,43]. Nowadays, exercise has been elevated to a new level with the main purpose of improving quality of life and medical treatment. In this new role, history has been recorded in many ancient works, both in the East and West, with famous physicians, thinkers, and philosophers such as Susruta (around 600 BC) in India, Hippocrates (460-370 BC) in Greece, and Galen (129-210 BC) in Rome. In modern medicine in the 18th century, the word "*Medicina Gymnastica: or a treatise concerning the power of exercise, concerning the economy: and the great necessity of it in the cure of several distempers*" was published in 1705 by the London physician, Francis Fuller. In 1927, the Harvard Fatigue Laboratory was established and after several decades of research, the field of Exercise Physiology began researching the importance of exercise for sports performance, physical and mental training, health, and injury recovery, and various recovery therapies have been widely recognized [44].

5.2. Collective exercise prevents many diseases

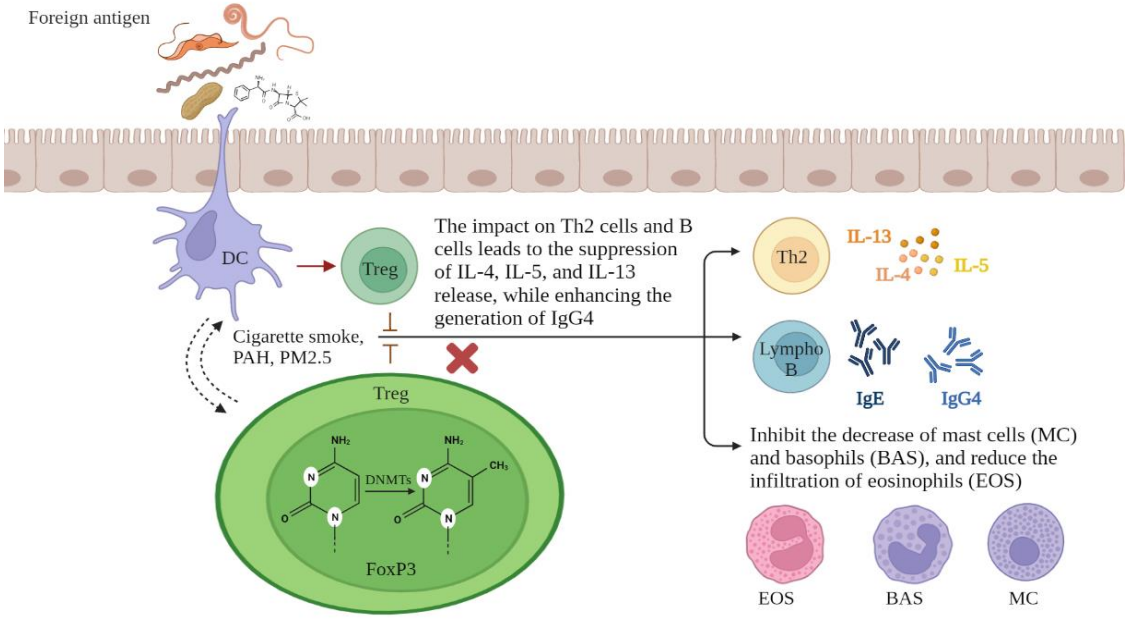

Figure 8. *Exposure to pollutants in the environment such as PM 2.5, PAH, etc., can lead to cytosine nucleotide methylation, inhibiting Treg function and altering the antibody balance of B cells between IgG4 /IgE [25].*

Several studies have indicated that high-frequency exercise alters gene structure, including the methylation/demethylation of DNA and changes to histone molecule structure affecting health outcomes [19]. Exposure to air pollution such as PM 2.5, CO, NO_2, and toxic compounds such as polycyclic aromatic hydrocarbons disrupts the balance between inflammatory cytokines in Th17 cells and anti-inflammatory cytokines in Treg cells, alters the antibody response of B lymphocytes, and leads to an increased risk of chronic disease, asthma, and allergies [25]. Exercise increases the process of DNA methylation, reducing the expression and inhibition of inflammatory cytokines, while also increasing the process of DNA demethylation, increasing the expression of anti-inflammatory cytokines such as IL-10 in Treg cells, helping to reduce the progression of chronic disease, asthma, and allergies in polluted environments (see Figure 8).

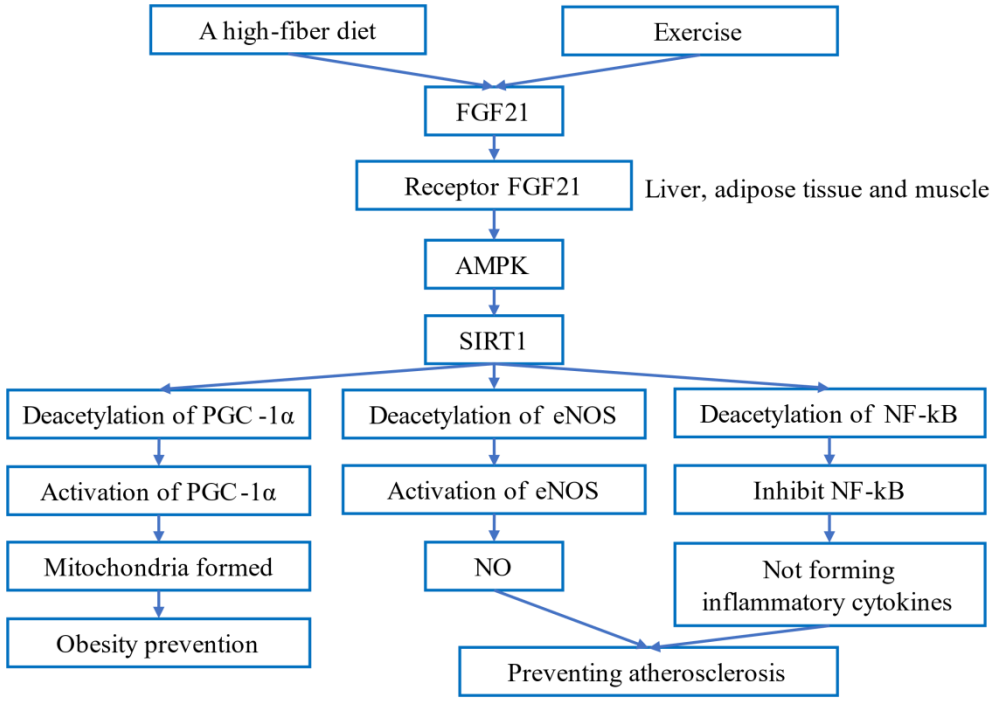

Figure 9. *The relationship between a high-fiber diet and exercise related to the FGF21-SIRT1 pathway helps prevent many diseases.*

In addition to a fiber-rich diet, exercise also increases FGF21, promoting the activity of SIRT1 through the FGF21 receptor of the signaling pathway [45,46]. SIRT1 promotes deacetylation of NF-kB, inhibiting the formation of inflammatory products, and deacetylation of PGC 1 α contributing to the activation of the formation of thermogenesis that helps to burn excess energy, converting white fat into brown fat to prevent obesity. Moreover, SIRT1 contributes to the deacetylation of eNOS dimer, promoting the formation of nitric oxide (NO) that causes dilation and increases the elasticity of blood vessels, helping to reduce resistance to blood flow, preventing the risk of high blood pressure and the formation of atherosclerotic plaques and blood clots that cause blockages in the heart and brain [47,48]. In summary, the

relationship between a fiber-rich diet and exercise is associated with the FGF21-SIRT1 pathway to prevent various diseases through the diagram presented in Figure 9.

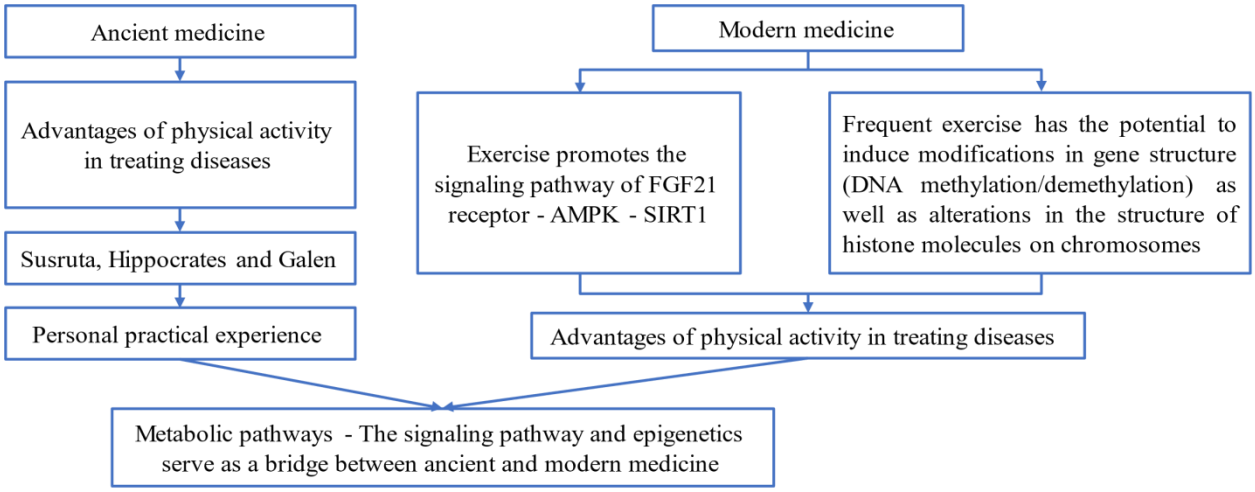

Figure 10. *Metabolic exchange - signaling pathways and epigenetics as a bridge between ancient and modern medicine.*

Based on the evidence presented, exercise is a simple but highly effective method for the treatment of non-communicable diseases. While ancient medicine had renowned physicians and thinkers such as Susruta, Hippocrates, and Galen who recognized the benefits of exercise in treating illnesses based on their personal experiences, modern medicine has shown that healthy exercise and diet can affect gene structure, signal transduction pathways, and metabolic exchange. Advances in epigenetics, signal transduction pathways, and metabolic exchange research have helped connect ancient and modern medicine in concluding that exercise is a method for improving health, mental well-being, and quality of life (see Figure 10).

VI. CONCLUSION

Throughout history, humans have progressed through various stages of mastering nature and improving society, from simply satisfying basic needs for survival to pursuing a more sophisticated and fulfilling lifestyle that includes invaluable spiritual values. However, current issues require attention and resolution that are not limited to both micro and macro scales. Past dietary and lifestyle behaviors were intended to meet survival needs, but today they need to be transformed to meet higher standards of health improvement and enhancement.

Furthermore, positive behaviors related to physical and mental health, such as regular exercise, optimistic thinking, and living in harmony with nature and society, also require proper attention. Only a comprehensive resolution of these aspects can improve the health foundation of Vietnamese people, in particular, and enhance human lifespan in general.

VII. PERSONAL OPINION

In the field of nutrition and food science, the prevalence of chronic diseases linked to highly processed food products and energy-dense, protein, sugar, and fat-rich industrialized meals that lack essential micronutrients is a significant concern. This issue needs to be emphasized to attract scientific research attention. From a social perspective, public attention needs to be focused on the appropriate selection of diets and scientifically-based food processing methods. Moreover, the proportion of protein, carbohydrate, fat, and fiber in meals needs to be viewed with a fresh perspective, not just the quantity. The dissemination and popularization of this knowledge is an urgent matter.

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