Review

Clin Ter 2023; 174 Suppl. 2 (6):209-213 doi: 10.7417/CT.2023.2489

Nutrigenomics: SNPs correlated to detoxification, antioxidant capacity and longevity

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Abstract

Nutritional genomics, also known as nutrigenomics, is the study of how a person's diet and genes interact with each other. The field of nutrigenomics aims to explain how common nutrients, food additives and preservatives can change the body's genetic balance towards either health or sickness. This study reviews the effects of SNPs on detoxification, antioxidant capacity, and longevity. SNPs are mutations that only change one nucleotide at a specific site in the DNA. Specific SNPs have been associated to a variety of biological processes, including detoxification, antioxidant capacity, and longevity. This article mainly focuses on the following genes: SOD2, AS3MT, CYP1A2, and ADORA2A (detoxification); LEPR, TCF7L2, KCNJ11, AMY1, and UCP3 (antioxidant capacity); FOXO3 and BPIFB4 (longevity). This review underlines that many genes—among which FOXO3, TCF7L2, LEPR, CYP1A2, ADORA2A, and SOD2—have a unique effect on a person's health, susceptibility to disease, and general well-being. Due to their important roles in numerous biological processes and their implications for health, these genes have undergone intensive research. Examining the SNPs in these genes can provide insight into how genetic variants affect individuals' responses to their environment, their likelihood of developing certain diseases, and their general state of health. ***Clin Ter 2023; 174 Suppl. 2 (6):209-213 doi: 10.7417/CT.2023.2489***

Key word: *SNPs, Nutrigenomics, longevity, detoxification, antioxidant*

Introduction

Nutrigenomics

Nutritional genomics is an emerging area of study that integrates the domains of nutrigenetics and nutrigenomics (1,2). Nutrigenomics holds the promise of yielding notable health advantages. However, despite the demand for medical geneticists being substantial, their availability is still limited. Furthermore, primary care physicians possess only basic training in nutrition and genetics (3). It is predicted that the human genome polymorphisms map will contribute to establishing optimal diets and understanding the role that nutrition plays in human health and disease. Together, advanced genetic research and nutrigenomics studies may help us in learning how our unique genetic makeup contributes to the emergence of polygenic diet-related disorders, including cancer and cardiovascular diseases. With the ultimate goal of customizing food and nutrition based on an individual's genotype, nutrigenomics perceives food as a major environmental element in the gene-environment interaction (4).

In this study, detoxification, antioxidant capability, and longevity are discussed in relation to polymorphisms. Protecting against potentially hazardous chemicals and oxidative stress, detoxification plays a crucial role in maintaining overall health. The term "detoxification" refers to the physiological process, through which the body neutralizes potentially hazardous chemicals or toxins, or prepares them for elimination. The liver, kidneys, lungs, and skin are the key organs involved in detoxification (5). Cell damage, inflammation, and diseases are all possible outcomes of oxidative stress (6). Longevity in humans results from a

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ISSN 1972-6007

dynamic interaction between genetic make-up and external stimuli. The heritability of longevity has been shown to be consistently low among many populations: both the aging and overall life span are heavily affected by our surroundings. To better inform public health efforts and promote population health, it is important to identify potential environmental determinants of longevity (7).

Polymorphisms and their possible effects on an individual's physiological status

Polymorphisms refer to variations in DNA sequence, the most prevalent kind of which is known as Single Nucleotide Polymorphism (SNP). Genetic variances can impact a person's disease risk, response to therapy, and overall health. There are several potential ways in which polymorphisms can affect physiological status; moreover, some polymorphisms have been related to an increased risk of contracting specific diseases (8). For example, the risk of getting breast and ovarian cancer is higher in people with certain SNPs in the BRCA1 and BRCA2 genes, immune system gene polymorphisms may contribute to the development of autoimmune disorders, and the way an individual reacts to a certain drug could be affected by a polymorphism. Polymorphisms have also been shown to alter metabolic pathways and the way nutrients are used by the body. Enzyme polymorphisms can result in a loss or gain of enzyme activity. This has the potential to influence numerous metabolic pathways and activities (9).

Health outcomes may be affected by the interaction between genetic variants and environmental variables. For example, changes in genes involved in cellular repair, stress response, and metabolism can have an effect on how quickly or slowly aging occur. Moreover, the genetic make-up of some people may make them more resistant to the effects of particular environmental stresses or, on the other hand, particular SNPs are linked to elevated disease risks. The body's inflammatory and immunological responses can be affected by genetic differences, which in turn affects susceptibility to infections and autoimmune diseases (10).

In short, health outcomes are determined by a complex relationship of genetic predisposition, environmental variables, and behavioral choices. Not all polymorphisms have clearly defined impacts, either, and genetics as a whole is always developing, as new studies reveal previously unknown factors that affect human health (11,12).

SNPs influence on detoxification and antioxidant capacity

Different biological functions, such as detoxification, antioxidant capability, and longevity, have been linked to particular SNPs. Genetics is simply one of the many factors that determine these characteristics, and our understanding of genetics is expanding all the time. Toxic chemicals are eliminated from the body by a physiological process, known as metabolic detoxification (13,14). The sensitivity of the body to both endogenous and exogenous toxins may be influenced by genetic variability and dietary variables, both of which can affect the action of detoxification enzymes (13,14). The influence of particular SNPs on detoxification and antioxidant capacity can differ significantly, depending on the gene expression and some environmental context. (13,15).

The process of detoxification is how the body breaks down and gets rid of toxic components, including poisons, medications, and pollution. By changing the activity of the enzymes responsible metabolizing and removing these chemicals, SNPs can impact the detoxification pathways. The cytochrome P450 (CYP) enzyme family, which helps

Table 1. SNPs, their gene and function correlated to detoxification and antioxidants.

RsID	Gene	Function	Alleles	wt/mt	References
rs4880	SOD2	Enzyme activity enhanced (about 33% higher)	T/T	wt/wt	(18-21)
		Enzyme activity enhanced (about 33% higher)	C/T	wt/mt	
		Typical	C/C	mt/mt	
rs3740393	AS3MT	Faster and more effective arsenic detoxification	C/C	mt/mt	(22,23)
		Typical	C/G	mt/wt	
		Typical	G/G	wt/wt	
rs72547515	CYP1A2	Decreased activity or inactive enzyme	A/A	mt/mt	(24-27)
		Decreased enzyme activity	A/G	mt/wt	
		Typical	G/G	wt/wt	
rs762551	CYP1A2	Faster metabolism of caffeine	A/A	wt/wt	(24,28,29)
		Typical	A/C	mt/wt	
		Slower metabolism of caffeine	C/C	mt/mt	
rs2298383	ADORA2A	No increase in anxiety from caffeine (in average amount)	T/T	wt/wt	(24,30-32)
		No increase in anxiety from caffeine (in average amount)	C/T	mt/wt	
		Probable increase in anxiety from caffeine	C/C	mt/mt	

in the metabolization of several substances, contains some crucial genes involved in detoxification (16).For instance, an SNP might cause an enzyme to have lesser activity, which would result in delayed chemical detoxification. On the other hand, some SNPs can cause hyperactive enzymes, which may increase the likelihood of negative reactions to specific medications or chemicals (16).

Catalase and antioxidant enzymes' activities can be changed by SNPs in their respective genes. This may raise the risk of a number of conditions linked to oxidative damage, including cancer, neurological disorders, and cardiovascular diseases. Genetic investigations, such as Genome-Wide Association investigations (GWAS), are frequently used to identify specific SNPs that are connected to detoxification and antioxidant-related processes (17). Table 1 reports the SNPs that are correlated to detoxification and antioxidants.

Table 1 summarizes the impact of different genetic variations (SNPs) on particular genes and their functions. Changes in enzyme activity, metabolite levels, and reactions to caffeine or anxiety brought on by specific metabolites are among the main function of these SNPs. For instance, the presence of specific alleles is linked to either higher or lower SOD2 enzyme activity in the case of rs4880 in the SOD2 gene. Similar effects of the allele appear to affect urine excretion of arsenic metabolites for rs3740393 in the AS3MT gene.

The CYP1A2 gene has variants (rs72547515 and rs762551) that affect how caffeine is metabolized. The pace at which caffeine is metabolized by different alleles influences how quickly or slowly it is metabolized in the whole body. Anxiety responses to coffee are linked to the rs2298383 SNP in the ADORA2A gene. Despite consuming large amounts of caffeine, some genotypes manifest no increase in anxiety, while others imply that large amounts of caffeine may increase anxiety. The explanations given here are based on the data in Table 1; nevertheless, for a more thorough understanding, it is advised to consult relevant scientific literature and molecular biology and genetics specialists (32).

SNPs influence on longevity

Research on increasing life expectancy is more commonly associated with the term "longevity," which can be alternatively thought of as "maximal lifespan". Life expectancy is affected by both genetics and environmental variables. As far as genetics are involved, longevity is likely affected by at least three distinct groups of SNPs. First of all, numerous SNPs are thought to affect susceptibility to diseases that shorten life expectancy. The second group is comped by SNPs that are common among elder people, thus appearing to increase longevity. Third, some SNPs may have an effect on one's lifespan only in specific environmental settings, such as those that shorten or increase lifespan only in people with a specific genotype who are also exposed to specific foods or pollutants (32). Table 2 reports the SNPs correlated to longevity.

Table 2 provides a list of genetic variations (RsIDs), their associated genes, and their effects. It is concluded that the genes FOXO3 and BPIFB4 play roles in longevity or long-lived qualities. The characteristics include those that increase the likelihood of living a long life and extending average or normal longevity. FOXO3 is a transcription factor and a member of the FOXO family, sharing the FHRE DNA consensus sequence. The FOXO3 SNP rs2802292 minor G-allele is closely linked to human longevity, and its copy number demonstrated a favorable correlation with decreased susceptibility to age-related diseases. If the BPIFB4 gene's rs2070325 is connected to "long-lived variant" and "typical longevity," this could imply that this genetic variation is linked to longer lifespans. It's crucial to remember that environmental conditions, interactions with other genes, and lifestyle choices can all have an impact on how genes affect longevity (33).

Discussion

Why study SNPs correlated to detoxification, antioxidant capacity and longevity

SNPs that are associated with lifespan, antioxidant capacity, and detoxification are an interesting subject of study, to learn more about numerous aspects of human health and ageing (33). For example, SNPs can affect how a person metabolizes medications and pollutants: by understanding the SNPs associated with detoxification pathways, a person's genetic composition can be taken into account when designing medical treatments and drug dosages (39). Detoxification pathways are essential for the body to digest and get rid of toxic chemicals, such as pollution, heavy metals, and carcinogens. Antioxidants are essential in the fight against oxidative stress, which has been related to ageing and a number of chronic diseases. Researchers can learn more about why certain people are more prone to oxidative damage and age-related disorders than others by studying SNPs that are associated with antioxidant enzymes and pathways. This information can direct interventions and way of life modifications to support better health and lifespan. Finding lifespan-linked SNPs can reveal information about the genetic causes of a longer, healthier life. By examining

Table 2. SNPs, their gene and function correlated to longevity.

RsID	Gene	Function	Alleles	wt/mt	References
		Increased odds of living longer	G/G	mt/mt	
		Increased odds of living longer	G/T	wt/mt	
rs2802292	FOXO3	Typical	T/T	wt/wt	(2,33-35)
		Long-lived variant	G/G	mt/mt	
		Typical longevity	A/G	wt/mt	
rs2070325	BPIFB4	Typical	A/A	wt/wt	(36-38)

these genetic markers, scientists can identify the processes and mechanisms that support healthy ageing and create interventions to support it (40).

Risks of low detoxification and antioxidant capacity

Having insufficient antioxidant and detoxifying ability might be harmful to one's health, since detoxification pathways and antioxidant systems are crucial in preventing oxidative stress, environmental contaminants, and the accumulation of dangerous chemicals in cells and tissues. Cellular damage, inflammation, and the emergence of several chronic diseases and neurological problems have all been linked to oxidative stress. Oxidative stress is also a significant contributor to ageing. A compromised detoxification system could result in the body storing harmful substances, which, together with oxidative stress, can harm the immune system's response. Moreover, cardiovascular diseases are often accompanied with inflammation and oxidative stress, because a decreased antioxidant capacity can raise the risk of cardiovascular issues. A low capacity for detoxification can make the breakdown and removal of toxins ineffective. Genetics, lifestyle choices, and environmental exposure all have a role in a person's capacity for detoxification and antioxidant defense (41).

Most important genes having SNPs involved in these mechanisms

This review would like to underline the importance of the genes SOD2, AS3MT, CYP1A2, and ADORA2A, which are involved in detoxification; genes LEPR, TCF7L2, KCNJ11, AMY1, and UCP3, concerning antioxidant capacity; and finally, the aforementioned FOXO3 and BPIFB4, which can affect longevity. This study came to the conclusion that all of these genes are significant, because they each have a unique effect on a person's health, susceptibility to disease, and general well-being. For example, longer lifespans and a lower chance of developing age-related disorders have been associated with variations in gene FOXO3. One of the most significant genes associated with the risk of type 2 diabetes is TCF7L2, whose variations significantly impact the control of insulin and glucose metabolism. Gene LEPR plays a role in metabolism and appetite control (41), so its SNPs might impact an individual's antioxidant capability and susceptibility to illnesses caused by oxidative damage. Due to their important roles in many biological processes and their implications for health, these genes have undergone intensive research (42). Examining these genes' SNPs can provide insight into how genetic variants affect how individuals respond to their environment, their likelihood of developing certain diseases, and their general state of health (43).

Outlook for Future Research

This review suggests that many genes and SNPs have a positive or negative effect on longevity and detoxification or antioxidant capacity, resulting in multiple effects on our organism. Future studies in nutrigenomics with a focus on SNPs linked to antioxidant capacity, detoxification, and lifespan have a great deal of potential to further extend our knowledge of individualized medicine, disease prevention, and ageing control. The study of SNPs in different cohorts could also be important to identify possible differences in detoxification, antioxidant capacity, and longevity in different populations.

Conclusions

Nutritional genomics is a new field of study, combining the former distinct fields of nutrigenetics and nutrigenomics. The key research areas include gene expression, protein and metabolite concentration, and consequently metabolism, health state, and disease risk. This covers the effects of dietary non-nutritive bioactive substances like enzyme inhibitors. Nutrigenomics may result in major potential health advantages. Currently, medical geneticists are in high demand, and yet are hard to come by because primary care doctors only have a basic understanding of nutrition and genetics. This study examines the effects of SNPS on detoxification, antioxidant capacity, and longevity, coming to the conclusion that SNPs are mutations that only affect one nucleotide at a specific site in the DNA. Specific SNPs have been associated to a variety of biological processes, including detoxification, antioxidant capacity, and longevity. This study concluded that all of these genes—FOXO3, TCF7L2, LEPR, CYP1A2, ADORA2A, and SOD2—are significant, because they each have a unique effect on a person's health, susceptibility to disease, and overall well-being.

Acknowledgements

This research was funded by the Provincia Autonoma di Trento in the framework of LP 6/99.

Conflicts of interest statement

Authors declare no conflict of interest.

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