Review

Clin Ter 2023; 174 Suppl. 2 (6):193-199 doi: 10.7417/CT.2023.2487

Nutrigenomics: SNPs correlated to minerals' deficiencies

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Abstract

Nutrigenetics and nutrigenomics are two interrelated fields that explore the influence of genetic diversity on nutrient responses and function. While nutrigenetics investigates the effects of hereditary genetic variations on micronutrient metabolism, nutrigenomics examines the intricate relationship between diet and the genome, studying how genetic variants impact nutrient intake and gene expression. These disciplines offer valuable insights into predicting and managing chronic diseases through personalized nutritional approaches.

Nutrigenomics employs cutting-edge genomics technologies to study nutrient-genome interactions. Key principles involve genetic variability among ethnic groups, affecting nutrient bioavailability and metabolism, and the influence of dietary choices based on cultural, geographic, and socioeconomic factors. Polymorphisms, particularly single-nucleotide polymorphisms (SNPs), significantly influence gene activity and are associated with specific phenotypes that are related to micronutrient deficiencies.

Minerals are inorganic elements, vital for various physiological functions. Understanding the SNPs associated with mineral deficiencies is crucial for assessing disease risk and developing personalized treatment plans. This knowledge can inform public health interventions, targeted screening programs, educational campaigns, and fortified food products to address deficiencies effectively. Nutrigenomics research has the potential to revolutionize clinical and nutritional practices, providing personalized recommendations, enhancing illness risk assessment, and advancing public health initiatives. Despite the need for further research, harnessing nutrigenomics' potential can lead to more focused and efficient methods for preventing and treating mineral deficiencies. ***Clin Ter 2023; 174 Suppl. 2 (6):193-199 doi: 10.7417/CT.2023.2487***

Key words: *Nutrients, SNPs, nutrigenomics, biomarkers, genes, minerals, calcium, potassium, iron, magnesium, selenium*

Introduction

The field of nutrigenetics studies the impact of genetic diversity on nutrient responses and functions. Although closely linked, nutrigenomics and nutrigenetics are not the same thing. Nutrigenetics investigates the effects of hereditary genetic variations on the uptake and metabolism of micronutrients, whereas nutrigenomics studies the connection between "diet and the genome with reference to nutritional effects on the metabolic, proteomic, transcriptional, and translational changes as well as dietary variation due to an individual's genetic background (1). Numerous chronic diseases can be predicted using nutrigenetic research; moreover, by using individualized nutritional management, these conditions may be avoided or treated more effectively. The majority of nutrigenetic experiments investigate how various polymorphisms influence alterations in eating patterns (2). Since people who carry certain polymorphisms in the apolipoprotein E gene are at a higher risk of myocardial infarction (MI), diets that are customized for such individuals should reduce the amount of saturated fats consumed in comparison to the conventional dietary guidance (3).

Through major metabolic capacity changes, brought about by diet over the history of human development, modern illnesses have become more prevalent. From an evolutionary standpoint, nutrition, like other environmental factors, is a limiting factor that places selective pressure on a population (4). A population's genotypes vary in their nutrient requirements. However, until these requirements (e.g., the need for additional calories from carbs and dietary fat) are addressed, the gene that transmits the high dietary requirement will continue to persist in the population. For example, this might apply to genes linked to diabetes and obesity (5).

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ISSN 1972-6007

To characterize the relationship between nutrients and genes, the term "Nutrigenomics" was coined. Physiology, biochemistry, metabolomics, proteomics, transcriptomics, and bioinformatics are all connected to genetics through nutrigenomics (6). In this developing discipline, cutting-edge genomics methods are used to examine how nutrients affect the genome and gene expression, as well as how genetic variations affect nutrient consumption: for example, numerous genetic variations have been shown to affect the way proteins are built and function. The study of how dietary factors affect people in different ways, according to their genetic makeup, is known as nutrigenetics, and it is a sub-field of dietary genome research. Nutrigenomics investigates how dietary factors interact with the genome to regulate modifications to proteins and other metabolic functions (7).

Nutrigenomics

The purpose of the developing field of nutrigenomics, which employs the most advanced genomics technologies available, is to examine the effects of vitamins on the genome and gene expression, as well as the effects of genetic variants on the intake of nutrients. Ethnic groups' genetic variability may have an impact on the bio-availability of nutrients and how they are metabolized (8), since the choice of food and its accessibility are largely based on cultural, geographic, and socioeconomic considerations. Because nutrition affects DNA sequences or even causes chromosomal instability, which results in abnormal gene dosage and undesired phenotypes, it also threatens the stability of the genome. As a result, the field of nutritional research known as "nutrigenomics" focuses on the application of molecular tools to the process of examining, assessing, and understanding the physiological reactions of certain populations or people to various diets (9).

The ability of particular nutrients to connect with transcription factors is necessary for these gene-nutrient interactions, which in turn control the attraction of RNA polymerase to promoter regions of genes and the amounts of transcripts that are generated as a result. For instance, research on fatty acids and vitamins A and D has shown that these nutrients effectively engage nuclear receptors and trigger gene transcription (10). Additionally, compounds like genistein (from soy) and resveratrol (from wine) indirectly affect numerous molecular signaling pathways through "nuclear factor kappa B," which ultimately results in the stimulation and control of important disease-related proteins (11).

Polymorphisms and their possible effects

In the context of genomics, the term "polymorphism" refers to the occurrence of two or more alternative variants of a certain DNA sequence in various individuals or populations. The most frequent kind of polymorphisms (also known as a single-nucleotide polymorphisms, or SNPs) involves variation at a single nucleotide; other polymorphisms can involve longer sections of DNA and thus be substantially larger (12). In the last two decades, nutrigenomics research has gathered enough information to distinguish between the phenotypes of SNPs in populations with and without micronutrient deficiencies. SNPs are the most frequent type of variation in human DNA (13), and can significantly affect gene activity (14).

Minerals and their role

Minerals are inorganic materials, necessary for the healthy operation of the human body and other living things. They are essential for many physiological functions and trace levels of them are needed for overall health and wellbeing (15). Major minerals (or "macro minerals") and trace minerals ("micro minerals") are two categories used to describe essential minerals: the first are needed in larger quantities, while the latter are needed in smaller ones. All of the necessary minerals should be present in a balanced diet (16).

The human body uses minerals in a variety of ways. For example, calcium is essential for the growth and upkeep of healthy bones and teeth, the immune system and energy generation both depend on iron, and magnesium is needed in countless metabolic processes. Potassium is an electrolyte that helps control fluid balance, neuron activity, and muscle contractions (16); while zinc participates in a variety of enzymatic processes and is essential for cell growth, wound healing, and immunological function. Iodine is required for the synthesis of thyroid hormones—which control growth, development, and metabolism—and selenium, thanks to its antioxidant properties, aids in preventing cell deterioration (17). The production of red blood cells, the development of connective tissue, and the functioning of the neurological and immunological systems all depend on copper. Each mineral serves a distinct purpose, so it is crucial to get enough of them through a balanced diet to preserve optimum health (18).

Why studying SNPs correlated to minerals deficiencies can be important

SNPs, which are variations in our DNA, can impact how our bodies absorb, transport, and use nutrients. Researchers can learn more about a person's genetic propensity for mineral deficiencies by analyzing the SNPs that are linked to these deficiencies, which are themselves linked to a higher risk of acquiring several illnesses. So, finding SNPs linked to mineral deficiencies can also help in the development of specialized treatment plans (19).

The field of nutrigenomics investigates the interactions between genes and nutrition and how they impact our health. For the purpose of developing public health interventions and policy, research on SNPs associated with mineral deficiencies can yield useful information. It helps in identifying population subgroups whose genetic make-up may make them more vulnerable to particular mineral deficiencies (20). To address and prevent deficiencies in susceptible populations, this knowledge can direct focused screening programs, educational campaigns, and the creation of fortified food products. Studying mineral deficiencies-associated SNPs can have a big impact on nutrigenomics research, individualized nutrition, illness risk assessment, treatment plans, and public

health initiatives (21). Moreover, it advances our knowledge of the genetic influences on mineral metabolism and creates opportunities for more focused and efficient methods to treat and prevent said deficiencies (22).

Calcium

Calcium is a necessary mineral, required for the upkeep of healthy bones and teeth. Additionally, it promotes healthy nerve transmission, blood coagulation, and hormone release.

Being involved in many cellular functions, calcium is important for overall health and wellbeing. Several foods—especially dairy goods like milk, cheese, and yogurt—are excellent providers of calcium. Muscle cramps and spasms, tingling in the fingers and toes, brittle bones, poor tooth health, and an increased risk of dental issues are just a few indications of a calcium deficiency, also known as hypocalcemia (23).

SNPs correlated to calcium deficiency and their effects

A person's chance of being calcium deficient can be affected by genetic factors affecting calcium metabolism. The gene for the vitamin D receptor is one of many SNPs connected to calcium metabolism. This SNP has been associated with variations in bone mineral density and calcium absorption, which may impact a person's vulnerability to calcium deficiency and associated diseases (24).

Dietary supplementation of calcium deficiency

Calcium supplements may be useful in cases of confirmed calcium deficiency or when its intake through food consumption is insufficient. Calcium supplements come in a variety of forms, including calcium citrate and calcium carbonate. To prevent potential adverse effects and guarantee proper absorption, it's crucial to adhere to the dosage and duration recommendations of healthcare professionals when using supplements. Supplements can be mixed with other nutrients, like vitamin D, which helps the body absorb calcium (25).

Table 1 gives details on a specific SNP (rs1800012) in the COL1A1 gene, the gene's function, the polymorphism's role, and the relevant alleles. Type I collagen, a kind of fibrillary collagen present in a variety of connective tissues, including cartilage, is mostly encoded by the COL1A1 gene. Collagen gives bones, tendons, ligaments, and other connective tissues structural support. Lower bone mineral density is linked to the COL1A1 gene variant or SNP (rs1800012).

Iron

Iron is a necessary mineral that is important for many bodily processes, including DNA synthesis, oxygen delivery, body energy production, immune system improvement, and cognitive growth. Both animal and plant-based foods contain iron (26): red meat, chicken, fish, shellfish, legumes, dark leafy greens, nuts, seeds, and grains and cereals are a few examples. Iron deficiency anemia is a disorder that can result from a lack of iron and that causes typical symptoms, such as weakness and exhaustion, shortness of breath, pale skin and nail beds, numbness in the hands and feet, and brittle nails (26).

SNPs correlated to iron deficiency and their effects

SNPs have an effect on iron metabolism and raise the risk of iron dysregulation (Table 2). Hereditary hemochromatosis, a condition marked by increased iron absorption and iron overload in the body, is linked to these mutations. However, it's crucial to remember that nutritional and environmental factors also play major roles in iron deficiency, and hereditary factors are only one component of this condition (27).

Dietary supplementation of iron deficiency

Under the direction of a healthcare practitioner, nutritional supplementation may be suggested in cases of iron deficiency. There are several types of iron supplements, and the selection of the correct one is influenced by many factors, including iron levels, toleration, and personal demands. It is thus crucial to seek medical advice in order to choose the right iron supplements and their dosage and duration. Following the suggested dosage is especially important, because also too much iron might have negative effects on health (28).

Magnesium

Magnesium is a necessary mineral that is vital to many body processes. For example, magnesium plays a role in the synthesis and storage of ATP, in muscle contraction and relaxation, in promoting the healthy functioning of the neural system and assisting in nerve transmission, and in maintaining strong bones by regulating calcium levels. Magnesium can be found in a number of foods, including vegetables with green leaves, seeds grains, fish and spinach. Magnesium deficiency symptoms include muscle cramps, fatigue, weakness, irregular heartbeat and palpitations, nausea, vomiting, and loss of appetite (31).

Table 1. SNPs related to calcium and their effects.

Calcium					
RsID	Gene	Polymorphism function	Alleles	wt/mt	Reference
rs1800012	COL1A1	Lower Bone Mineral Density	A/A	mt/mt	(23-25)
		Lower Bone Mineral Density	A/C	wt/mt	
		Typical	C/C	wt/wt	

Table 2. SNPs related to iron and their effects.

Iron					
RsID	Gene	Polymorphism function	Alleles	wt/mt	Reference
rs17342717	SLC17A1	Higher ferritin.	T/T	mt/mt	(26)
		Higher ferritin.	C/T	wt/mt	
		Typical	C/C	wt/wt	
rs1800562	HFE	High ferritin levels.	A/A	mt/mt	(27)
		Increased ferritin levels.	A/G	wt/mt	
		Typical	G/G	wt/wt	
rs855791	TMPRSS6	Lower ferritin levels.	A/A	mt/mt	(28)
		Lower ferritin levels.	G/A	wt/mt	
		Typical	G/G	wt/wt	
rs3923809	BTBD9	Higher ferritin.	G/G	mt/mt	(29)
		Higher ferritin.	A/G	wt/mt	
		Typical	A/A	wt/wt	
rs7385804	TFR2	Lower serum iron.	C/C	mt/mt	(26,27,30)
		Lower serum iron.	A/C	wt/mt	
		Typical	A/A	wt/wt	
rs3811647	TF	Higher ferritin.	A/A	mt/mt	(23-25)
		Higher ferritin.	A/G	wt/mt	
		Typical	G/G	wt/wt	

SNPs correlated to magnesium deficiency and their effects

SNPs have the potential to affect magnesium metabolism and cause magnesium deficiency. Lower amounts of magnesium in the body may result from polymorphisms that influence magnesium absorption and reabsorption. However, it is crucial to remember that also nutritional and environmental factors, in addition to genetic ones, play a big part in magnesium shortage (32).

Dietary supplementation of magnesium deficiency

Under the direction of a healthcare expert, nutritional supplementation may be suggested in cases of magnesium insufficiency. There are several types of magnesium supplements, including magnesium oxide, magnesium citrate, and magnesium glycinate. The selection of a supplement is influenced by things like absorption, toleration, and individual requirements (33).

The consequences of particular SNPs connected to magnesium are detailed in Table 3.

Selenium

Selenium is a trace mineral, essential for many physiological activities. The human body uses selenium for a variety of purposes, including antioxidant activity, thyroid and immunological functions, reproductive health, DNA synthesis and repair, and cognitive function. Brazil nuts, shellfish, meat and poultry, whole grains, milk and yogurt, eggs, lentils, and other seeds are among the foods that contain selenium. Deficiency signs can include mood swings, hair loss, increased susceptibility to infections, weakened immune system, thyroid malfunction, and muscle weakness and weariness (37).

SNPs correlated to Selenium deficiency and their effects

The metabolism of selenium and its possible effect on deficiency have been linked to SNPs (Table 4). Variations in these genes may have an impact on the expression or activity of selenium-related enzymes, which may have an impact on selenium status and associated health effects. However, the effects of these SNPs may differ between people, and more study is required to properly comprehend their implications (37).

Dietary supplementation of selenium deficiency

If dietary selenium requirements cannot be satisfied by diet alone, or if a person has a confirmed lack of the mineral, taking selenium supplements may be advised. To prevent an excessive intake of selenium, which can be dangerous, a healthcare practitioner should decide on the right quantity and duration of supplementation, based on each patient's needs and lab tests. A medical expert should be consulted before beginning any supplements regimen, since they can offer individualized advice based on certain health issues and factors (38).

Zinc

Zinc is a mineral that is part of numerous enzymatic complexes and is necessary for the proper functioning of many hormones, including insulin, growth hormone, and

Table 3. SNPs related to magnesium and their effects.

Magnesium					
RsID	Gene	Polymorphism function	Alleles	wt/mt	Reference
rs3750425	TRPM6	Lower serum magnesium levels; increased risk of hypomagnesia with proton pump inhibitors.	T/T	mt/mt	(31-33)
		Lower serum magnesium levels; increased risk of hypomagnesia with proton pump inhibitors.	C/T	wt/mt	
		Typical	C/C	wt/wt	
rs12255372	TRPM6	Lower magnesium levels on average; increased risk of hypomagnesia with proton pump inhibitors.	C/C	mt/mt	(31-33)
		Lower magnesium levels on average; increased risk of hypomagnesia with proton pump inhibitors.	C/T	wt/mt	
		Typical	T/T	wt/wt	
rs11191548	CNNM2	Higher levels of 25-hydroxyvitamin D (main circulating form of vitamin D)	C/C	mt/mt	(34-36)
		Higher levels of 25-hydroxyvitamin D (main circulating form of vitamin D)	C/T	wt/mt	
		Typical	T/T	wt/wt	

sex hormones. Zinc is present in various foods: fish and meat, grains, legumes, nuts, and seeds. The Recommended Daily Intake is 11 mg per day for men, while for pregnant and lactating women it is 13 mg per day (39).

SNPs correlated to zinc deficiency and their effects

Several SNPs have been identified that are associated with zinc metabolism and homeostasis, influencing the risk of developing zinc deficiency. These SNPs primarily affect genes involved in zinc transport, absorption, and utilization within the body.

One such SNP is found in the SLC39A8 gene (Table 5), encoding a zinc transporter responsible for facilitating zinc uptake into cells. Variants of this gene have been linked to altered zinc levels and potential zinc deficiency due to impaired transport. Another SNP in the SLC30A8 gene, which encodes a zinc transporter involved in insulin production, has been associated with both reduced zinc levels and an increased risk of type 2 diabetes (40,41).

Zinc deficiency plays a crucial role in various physiological processes, including immune function, growth, wound healing, and cognitive development. Individuals with SNPs related to zinc deficiency may be more susceptible to immune system dysfunction, impaired wound healing, and cognitive deficits. Additionally, zinc deficiency has been associated with increased susceptibility to infections, impaired taste and smell perception, and skin issues (42).

Dietary supplementation of selenium deficiency

Dietary supplementation is a key strategy to address zinc deficiency. Aiming to meet the recommended dietary allowances for zinc can help prevent and alleviate the adverse effects of deficiency. However, in cases where genetic variations predispose individuals to zinc deficiency, targeted supplementation might be beneficial. Supplementing with zinc in cases of genetically influenced deficiency can support immune function, aid wound healing, and promote overall health. Zinc supplements are available in various forms, such as zinc gluconate, zinc sulfate, and zinc citrate. It's important to note that excessive zinc supplementation can lead to adverse effects, including impaired copper absorption and gastrointestinal disturbances (42,43).

Conclusions

Many genetic polymorphisms can influence the levels of minerals in the human organism, modifying the nutritional and health status of the individual. Although further research

Table 4. SNPs related to selenium and their effects.

Selenium					
RsID	Gene	Polymorphism function	Alleles	wt/mt	Reference
rs3877899	SELENOP	Lower serum selenium levels	T/T	mt/mt	(37,38)
		Lower serum selenium levels	C/T	wt/mt	
		Typical	C/C	wt/wt	

Table 5. SNPs related to zinc and their effects.

Zinc					
RsID	Gene	Polymorphism function	Alleles	wt/mt	Reference
Rs13266634	SLC30A8	Lower zinc level, increased glucose levels in blood	C/C	mt/mt	(40,41)
		Lower zinc level, increased glucose levels in blood	C/T	wt/mt	
		Typical	T/T	wt/wt	

is needed to identify possible new SNPs correlated to minerals' absorption, transport, and metabolism, the study of nutrigenomics can be exploited in clinical and nutritional practices to provide tailored suggestions.

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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