Leveraging Nutrigenetic Science
To Empower Precision Nutrition

Co-founders:
Dr. Daniel Wallerstorfer PhD, Rootine CTO
Rachel Sanders MBA, Rootine CEO

Introduction

The vitamin and supplement industry is plagued with confusion and controversy, stemming from the lack of scientific research, inability to customize products, lack of quality control, and the overarching view that generic recommendations around nutrition and supplementation are effective across unique populations.

As scientists and nutrition experts, we know this to be incorrect: generic recommendations are not adequate. Each person is inherently different, from their DNA to their diet, so it makes logical sense that “optimal” nutrition varies widely from person to person. In fact, studies have shown that even identical twins differ from mutations in their immune systems [1]. As such, generic recommendations for nutrition and supplementation simply do not apply. With certainty, there is no “best diet” for humans.

At Rootine, we set out with a different approach - one that is focused on utilizing in-depth scientific research and relevant personal health data to create high-quality, science-backed, personalized health and wellness products.

Though a rapidly expanding field, the basis of genetic research shows that DNA analysis can inform health and lifestyle decisions that may encourage long-term wellbeing. For this reason, genetic analysis forms the basis for much of the product development at Rootine.

Rootine’s team is made up of genetic scientists, biotechnologists, health professionals, and nutrition experts. We want to share our expertise on genetics and how genetic variation influences the individuality of health and nutrition needs.
How Genes Influence Our Health

Genetics 101

The human body consists of approximately 50 trillion cells, with hundreds of cell types to perform unique functions. The genetic code controls cellular differentiation and determines which cells will become bone, muscle, blood, and so on. The bone cells keep our skeletal system strong; muscle cells help us move and pump blood; and blood cells transport oxygen throughout the body. Almost every cell has a nucleus that contains chromosomes, which are made up of genes. Genes tell these cells what to do; they are the specific recipe that tells our body how to function.

Genes are made up of DNA (deoxyribonucleic acid). If each gene is a recipe, the DNA molecules are the words of that recipe. DNA is made up of a set of letters - A, T, G, C - all representing molecules (Adenine, Thymine, Cytosine, Guanine) that combine in groups of 2 to form base pairs.

The order of the letters is very important, as it tells the genes how to function. Each gene usually has a single function. For example, some genes tell the body how to color the iris and differences in these genes produce different eye colors. Every function of the body is controlled by one or more genes, including the way we break down food, metabolize medication, or mount an immune response to a pathogen.
The genetic code of a human being consists of 3.2 billion base pairs. They are split into 23 "packages" called chromosomes and, on average, a chromosome contains about 1000 different genes.

**Genetic Variants**

Our genes are not completely error-free. In order to grow, our cells divide and copy to make more cells. The DNA copying process is not perfect, and can sometimes produce errors. The body has built-in mechanisms to catch and fix these errors, but occasionally mistakes are made and a genetic variant makes it through.

As cells continue to copy, these errors become permanent fixtures in our bodies, creating genetic variations. Genetic variants are the parts of DNA that differ from person to person and make us unique. They can occur throughout a person's lifetime or be passed from one generation to the next. Parents can pass their variants to their children if the genetic variant occurs in the sperm or egg cells.

While external influences can affect individual genes and disrupt their function, the majority of our defective genes are inherited from our parents. Each embryo receives approximately half of its genes from the father and half of its genes from the mother, resulting in a new human being with some of the characteristics of each parent. Whether a genetic variant is passed on, is determined randomly, so it is possible that one sibling will carry a variant while others do one.

**Impact Of Genetic Variants On The Body**

Many genetic variants cause no harm and often go undetected. Other variations, or mutations, cause catastrophic consequences and lead to the death of the cell, and are rarely passed from one generation to another. However, there are some genetic variants that can cause cells to function differently or incorrectly. This can contribute to different traits or increased risk for certain diseases.

Some genetic variants have developed with the population over time as they helped our ancestors live in the ancient world. In some cases, these previously positive gene variants have negative effects in the modern environment. For example, the link between the sweet taste of sugar identifying readily available and safe calories (sweet plant foods, like fruit, tend to be safe and not be poisonous compared to bitter tasting plant foods) likely exerted evolutionary pressure for humans to prefer the sweet flavor. [169] In the past, this adaptation meant the human had a better chance of surviving; however, in the modern world, this trait can be harmful because hyper-palatable and sugar-laden foods are plentiful and have been linked to weight gain and associated chronic disease risk.
Certain genetic variants have even more profound effects on health, increasing the risk of heart attacks, triggering asthma and allergies, causing lactose intolerance and many other disorders. While some genetic variants lead to inevitable health conditions, most genetic variants simply increase the overall risk of developing a disease.

For example, a person may have genetic variants that increase their risk for diabetes. However, not everyone at risk for diabetes actually develops the disease. Furthermore, even people with a high risk of diabetes can lower their risk through lifestyle changes, like diet and exercise, preventative medication, and some targeted supplemental nutrients. In these cases, knowledge is power and understanding a predisposed health risk can alert the individual to take enhanced proactive measures.

Other genetic traits only cause illness when they interact with a specific environmental feature. For example, lactose intolerance is a genetic condition that causes a person who drinks milk (or consumes lactose-containing products) to have digestive issues. A lactose-intolerant person who does not consume these products will not have any symptoms. Again, this genetic understanding can be incredibly beneficial to the individual and help guide daily decisions.

Genetic Testing and Analysis

One type of genetic variant is called a SNP (single nucleotide polymorphism), which is a change of a single DNA base. For example, some people may have an A in a specific location while other people may have a T.

As previously stated; genetic variants can be silent and have no effect on the body; genetic variants can have catastrophic consequences and lead to death or a serious disease; or genetic variants can fall in the middle ground of severity, where they lead to a slight modification of the final gene product and affect its function. These SNPs act as “sign-posts” and accurately identify if the individual carries the variant version of the gene.

Thanks to the latest research and technologies, it is now possible to affordably, accurately, and quickly test specific SNPs to determine personal health risks and strengths. In many cases, taking advantage of this knowledge, and following some precautionary measures, health risks may be mitigated. This is the next step in preventive and personalized medicine, and signals a new generation of health care.

Genetics and Nutrition: The Research

Food and nutrition have been studied for centuries but modern nutritional science is relatively new. After the first vitamin was identified in 1926, scientists spent the better part of the 20th century studying the impact of single nutrient deficiencies on the body. Since the early 2000s,
research on the role of nutrition in complex diseases like diabetes, heart disease, and cancer has accelerated. [2]

Much of this research does not account for genetic sub-groups, but rather focuses on average responses to nutrients across stratified populations, including both individuals with and without genetic variants. This approach creates nutritional guidelines (e.g. recommended dietary allowances (RDAs)) that assume population homogeneity and can pose potential harm for people with certain genetic variations [3].

With the advancement of genetic testing technology and the resulting increase in the readily available genetic data, there is an increase in research investigating how genes interact with nutrient metabolism and how genetic variation affects health risks.

This complex interplay between nutrition and the human genome has created new sub areas of research: nutrigenetics and nutrigenomics. Nutrigenetics is the study of the modifying effects of variations in nutrition-related genes on micronutrient uptake and metabolism, and the related effects on health. [63] Nutrigenomics harnesses multiple disciplines, including dietary effects on genome stability, epigenome alterations, transcriptomics, proteomics, and metabolomics to diagnose health status and/or disease trajectory.

These areas of research are important because it has become increasingly evident that (a) risk for disease increases with DNA damage (which is dependant on nutrition status), (b) optimal daily micronutrient intake is dependent on genetic variants, and (c) genetic variation influences the metabolic response to dietary nutrients. [4] This science enables clinicians to make nutrition and supplementation recommendations that are targeted to each individual, rather than relying on populational research that does not take genetics into account.

Harvard health notes that these new fields of study have, “opened the door to precision nutrition - the creation of individualized eating plans based on a person’s genome,” ushering in the future of nutritional science and clinical care. [63 & 5]

**Identifying High-Quality Research**

Since genetic science is a rapidly evolving field, study quality is of the utmost importance in determining relevance. The gold standard for research studies are peer reviewed studies performed outside of specific organizations (or independently). It is also important that these studies are repeatable with similar results across various study populations and researchers.

The National Center for Biotechnology Information (NCBI), defines peer review as “a process of subjecting an author’s scholarly work, research or ideas to the scrutiny of others who are experts in the same field.”
The NCBI states that the peer review process encourages high standards and notes that "Within the scientific community, peer review has become an essential component of the academic writing process. It ensures that papers published in scientific journals answer meaningful research questions and draw accurate conclusions based on professionally executed experimentation. The major advantage of a peer review process is that peer-reviewed articles provide a trusted form of scientific communication. Since scientific knowledge is cumulative and builds on itself, this trust is particularly important." [6]

**How To Read Research**

No single study should be taken in isolation. It is well known in the science community that a single study can be found to say virtually anything due to the sheer volume of research that has been completed over the decades. For this reason, it is necessary to ensure there are multiple studies across multiple populations all with the same (or similar findings).

Study repetition in general, and especially across new cohorts, populations, and researches, ensures that the results are accurate and consistent. This helps to prevent unknown bias, unknown study error, and unknown abnormalities in the study cohort or testing method.

**Genetics + Nutrition: Summary of Research Findings**

The totality of nutrigenetic and nutrigenomic peer-reviewed research shows that when determining optimal strategies for both diet and supplementation, your DNA matters. This is due to the fact that differences in gene function caused by genetic variation from person-to-person (1) create differences in nutrition requirements and (2) contribute to the differences in the way certain nutrients interact with the body.

A bidirectional relationship exists between nutrition and the human genome. This interaction impacts both gene expression and metabolic response to nutrients, which can positively or negatively influence an individual’s health and susceptibility to disease [7]. An individual’s genotype can define nutrient status, metabolic response, and susceptibility to nutrient-dependent or related health disorders [4]. In addition, dietary nutrients regulate gene expression which influence cellular metabolism at the molecular level [9].

The current science clearly shows that inherited genetic variation has a prominent role characterizing an individual’s disease risk, nutrient needs, and metabolic response to bioactive compounds found in the diet and nutritional therapies. By clarifying and emphasizing the importance of genetics on each individual’s nutrient intake, nutrient status, and disease risk, we aim to harness this biometric data and leverage it to improve product efficacy, safety, and reliability [9].
When considered in relation to nutrition, genetic variability may be at least partly responsible for differences between individuals in: Absorption of food, metabolism, enzyme digestion, biosynthesis, catabolism, transport across cell membranes, uptake by cell receptors, storage, and excretion [3]. Genetic variations may also be linked to individual food likes and dislikes, potentially leading to lower intake of certain food groups and nutritional benefits.

In relation to weight, studies have shown that approximately 60% to 80% of excessive weight is heritable. In other words it is given to us by our parents in the form of genes. So it is more difficult for some people to maintain an optimal body weight than it is for others. Additionally, genetic variants inform how individuals may gain and/or lose weight. Some gain weight when following a diet with a high fat content while for others the fat content seems to play no significant role. Some people lose weight very quickly with regular exercise, while others hardly see any results from the same amount of effort.

How Genetics Influence Product Development at Rootine

It is a well-known fact that diet affects health; nutrition can contribute to specific diseases both directly and indirectly. New research shows that genetics impact both (1) each individual’s demand for particular nutrients and (2) risk factors for specific diseases that are impacted by nutrition. Therefore, it is imperative to take genetics into account when creating a plan around optimal nutrition. [160]

For this reason, we carefully consider genetics when creating our products. In addition to genetics, research also shows that genetics is only one factor to consider when understanding nutritional needs and underlying health conditions. That is why Routine also considers other biometric data; like blood levels and lifestyle information to create a complete and accurate understanding of each person’s unique needs

Rootine’s Daily Nutrient Packs

Rootine incorporates each subscriber’s genetic data in two ways: (1) we analyze specific genetic variants that have a one-to-one impact on an individual’s demand for a specific nutrient, and (2) we analyze genetic variants that influence categorical health risk (i.e. “heart health”) and determine the nutrients needed to help minimize that risk.

After review of all genetic analysis, Rootine then combines the findings with data on blood nutrient levels and lifestyle to create an optimal nutrient recipe for each individual.

(1) Analyzing genetic variants with a one-to-one impact on nutrient demands [brief overview]
<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Folate (Vitamin B9)</th>
<th>Vitamin D</th>
<th>Calcium</th>
<th>Iron</th>
<th>CoQ10</th>
<th>Selenium</th>
<th>Omega-3s</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gene</td>
<td>MTHFR</td>
<td>YDR</td>
<td>LCT</td>
<td>HFE</td>
<td>NQO1</td>
<td>GPX1</td>
<td>APOA1</td>
</tr>
<tr>
<td>rsID(s)</td>
<td>rs1801133 rs1801131</td>
<td>rs4988235</td>
<td>rs1800562 rs1799945 rs1800730</td>
<td>rs1800566</td>
<td>rs1050450</td>
<td>rs670</td>
<td></td>
</tr>
<tr>
<td>Approximate Prevalence</td>
<td>41% hetero - 9% homozygous</td>
<td>43% hetero - 7% homozygous</td>
<td>11% of population has homozygous requirement for risk</td>
<td>8% of the population cannot digest lactose in adulthood</td>
<td>0.5% of the population has combination of gene variants to induce genetic homocystinosis</td>
<td>4% of the population has total enzyme dysfunction and 40% have low enzyme efficiency</td>
<td>38% of the population has increased risk for oxidative stress due to limited glutathione reductase capacity</td>
</tr>
<tr>
<td>Normal Function</td>
<td>Codes for the enzyme responsible for the final step in converting folic acid and dietary folic acids into the biologically active form (5-MTHF)</td>
<td>The vitamin D receptor (VDR), is a nuclear receptor transcription factor which calcium (active vitamin D) binds to induce the expression of specific genes.</td>
<td>Produces the lactase enzyme that breaks down lactose (a natural sugar in dairy) into galactose and glucose</td>
<td>The HFE protein interacts with the transferrin receptor (TfR). Its primary mode of action is the regulation of the iron storage hormone hepcidin</td>
<td>NGO1 codes for the enzyme (NADPH oxidase) that converts CoQ10 (ubiquinone) into its active form (ubiquinol)</td>
<td>Codes for the glutathione peroxidase 1 enzyme that is considered a &quot;master antioxidant&quot; and detoxifies peroxides, notably hydrogen peroxide</td>
<td>66% of the population with genetic predisposition to HDL-lowering from increased omega-3 consumption</td>
</tr>
<tr>
<td>Effect of Variation</td>
<td>These SNPs reduce MTHFR conversion efficiency by ~35% per rs1801133 copy and ~20% per rs1801131 copy</td>
<td>Slight changes to the structure of the vitamin D receptor making binding to calcitriol less efficient, thus requiring super-physiologic levels of vitamin D to meet the same level of activation</td>
<td>Causes adult lactose intolerance and those affected are likely to avoid dairy products and intake 280mg less calcium per day than wild-type</td>
<td>Disrupts the ability to regulate uptake of iron resulting in increased intestinal iron absorption.</td>
<td>Gene variant heterozygotes have a reduced conversion efficiency of ubiquinone into ubiquinol and homozygotes have fully dysfunctional enzyme</td>
<td>Glutathione peroxidase 1 enzyme is less efficient, requiring more total active molecules to achieve normal level of oxidative stress</td>
<td>This variant results in in an HDL-lowering effect in the presence of increased omega-3 intake</td>
</tr>
<tr>
<td>Solution</td>
<td>Compensate for enzyme inefficiency with equal percent of folate RDA as pre-activated 5-methylfolate (5-MTHF).</td>
<td>Increase vitamin D by ~2x compared to the norm</td>
<td>Supplement with 280mg of calcium to compensate for reduced dietary intake</td>
<td>Consult your physician but typical solutions include 1) avoid iron supplements, 2) limit iron containing foods, 3) regular blood donations may be required.</td>
<td>Additional non-CoQ10 antioxidants to compensate for reduced capacity to handle ROS</td>
<td>Additional selenium needed</td>
<td>Phytosterols, instead of omega-3s, to improve blood lipid levels</td>
</tr>
</tbody>
</table>
● Selenium (GPX1)

Selenium is a trace element that your body needs to build essential proteins. One such protein is GPX-1, an enzyme (glutathione peroxidase) acting as a defense mechanism against certain damaging free radicals. If the body has sufficient selenium, it can produce these enzymes in sufficient amounts which helps to mitigate oxidative stress. However, certain individuals carry a genetic variation that reduces the efficiency of these enzymes to neutralize free radicals. Studies have found that increasing selenium intake above normal can activate more of these enzymes and establish a similar level of oxidative stress protection compared to normal non-variant carries. As a consequence of mutations in the GPX1 gene, some people require more selenium than others. [10 - 19]

● Omega 3 (APOA1)

Omega-3 fatty acids are considered “healthy” fats that are common in fish and in certain plant oils. Many people take omega-3 supplements and incorporate omega-3 rich foods into their diet because they are considered to be good for their cholesterol levels and contribute to a normally functioning heart. Studies have shown that this is indeed the case, but only if these people carry a certain version of the APOA1 gene. If they carry an APOA1 variant, HDL (the good cholesterol) levels actually worsen with additional omega-3 intake. Depending on the person’s genetics increasing omega-3 intake can either be positive or negative for a person’s HDL cholesterol levels. For APOA1 gene variant carriers, “phytosterols” may be a better solution for improving cholesterol levels. [20 - 22]

● Methylfolate (MTHFR)

Dietary folates and folic acid (synthetic form) are considered vitamin B9, a vital nutrient for proper fetal development, methylation, and homocysteine regulation. The importance of B9 was qualified when much of the food supply was fortified with folic acid. However, folic acid and most dietary folates must be converted into the active form to carry out the function of vitamin B9 and confer benefit. This activation is performed by the MTHFR gene product. Many variations in this gene exist; however, only two are considered impactful enough to alter bioactive folate status. These SNPs reduce the efficiency of the MTHFR enzyme and impair the body’s ability to activate folate. As a well documented gene-nutrient interaction, there is a clear understanding of how each mutation impacts the efficiency of the enzyme. Depending on the individual’s genetics, the optimal approach is to substitute an inverse percentage of the RDA as pre-activated folate (methylfolate) as the enzyme efficiency is impaired due to genetic variation. Thus, if the enzyme is operating at 60% efficiency, the individual would receive 40% of their folate dose as methylfolate and can maintain 60% of their RDA as folic acid. [47 - 62]
Co-Enzyme Q10 (NQO1)

Coenzyme Q10 is a strong antioxidant that is capable of neutralizing free radicals and supporting mitochondrial function, but only after being transformed into its active form, ubiquinol. This process is completed by the NQO1 gene product, an enzyme called NAD(P)H Quinone Dehydrogenase 1. If this gene does not function, coenzyme Q10 cannot be transformed into ubiquinol and it does not confer protection against free radicals. Therefore, it is important to know if your body is capable of activating coenzyme Q10 to determine your need to take additional antioxidants, or if CoQ10 supplementation is an effective strategy. [23, 24, 157 - 159]

Iron (HFE)

Iron is important to build the oxygen carrying hemoglobin in our blood. As the body has no reliable iron secretion mechanism to reduce iron load, uptake from food is carefully controlled by certain genes. Some people have inherited genetic variations in the related genes, which can lead to excessive iron uptake from food and iron-containing supplements. Too much iron can lead to iron overload syndrome, liver damage, and cancer. It is recommended that carriers of these genetic variations should not take extra iron in the form of supplements and may be required to modify their diet, with consultation from their doctor. [25 - 28]

Calcium (LCT)

Calcium is an important mineral that we need to absorb from our nutrition. It is present in a number of food types such as dairy products and certain vegetables, like broccoli. Scientific studies have shown that people with a certain genetic variation in a specific
gene (LCT) cannot digest lactose in adulthood and are considered lactose-intolerant. These people experience gastrointestinal discomfort when consuming products containing lactose, commonly found in dairy products. As dairy is a significant source of calcium for many people, studies have shown that those with variations in the LCT gene typically ingest on average 280mg less calcium per day than people without this variation. [29-32]

(2) Analyzing genetic variants that influence categorical health risk and determining the nutrients needed to help minimize that risk

The genetic impact on broader health categories is more complex, and (in most cases) requires a review of multiple genetic variations to understand the types of nutrients an individual may need to support each category. Rootine examines all relevant genetic variations supported by sufficient research, creates an overall "score" based on findings, and makes nutrient recommendations accordingly.

Our review is based on the understanding that if genetic variants make an individual more susceptible to certain health conditions, and improving nutrition may prevent those health conditions in the future.

<table>
<thead>
<tr>
<th>Category</th>
<th>Bone Health</th>
<th>Oxidative Stress</th>
<th>Detoxification</th>
<th>Heart Health</th>
<th>Cognitive Health</th>
<th>Metabolism Health</th>
<th>Joint Health</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genes</td>
<td>Col1A1, VDR, ESR1, LCT</td>
<td>GSTM1, GSTT1, GSTP1, SOD2</td>
<td>GSTM1, GSTT1, GSTP1</td>
<td>APOA1, APOAS, APOB, CDH13, CHDSB, NOS3, PON1, MTRR, MMP3, GJA4, ITGB3, CETP, MTHFR, NOS1AP, AGT, ADRB1, GNB3</td>
<td>APOE(1), APOE(2)</td>
<td>FTO, HHD1C, IL10, IL6, KCN711, PPARG, TCF7L2</td>
<td>TNFa, IL1a</td>
</tr>
<tr>
<td>Genes</td>
<td>Calcium, Vitamin D, Magnesium</td>
<td>Vitamin C and E, Alpha Lipoic Acid, Selenium, Zinc, CoQ10</td>
<td>Calcium, Selenium, Zinc, Iron</td>
<td>Magnesium, Vitamins B6, B9, B12, CoQ10, and Phytosterols</td>
<td>Vitamin A, C, E, B2, B6, B9 (Folate), B12, Alpha Lipoic Acid, Manganese, Selenium, Zinc</td>
<td>Vitamins A, C, E, B2, B6, B9 (Folate), B12, Alpha Lipoic Acid, Manganese, Selenium, Zinc, Calcium, Iron, Copper</td>
<td>Omega-3s, Methylsulfonylmethane</td>
</tr>
</tbody>
</table>

(continued on the next page)
- **Bone Health (Col1A1, VDR, ESR1, LCT)**

  There are many factors that affect the strength and health of your bones. Your genes play an important role, since genetic variations may lead to a faster loss of mineral density of your bones, due to impaired vitamin D function and reduced calcium intake, among others. Supplementing with the right type and amount of related nutrients can help you maintain good bone health. [33 - 46]

- **Metabolism Health (FTO, HHEX, HIGD1C, IL10, IL6, KCNJ11, PPARG, TCF7L2)**

  A healthy metabolism relies on several factors, including your genetics. Certain genetic variations may lead to a metabolism that has problems maintaining healthy blood sugar and inflammation levels. In these cases, supplementing with the right nutrients, specifically B vitamins, targeted minerals, and various antioxidant nutrients, can promote a healthy metabolism. [64 - 85]

- **Detoxification Ability (GSTM1, GSTT1, GSTP1)**

  We are continuously exposed to toxins through our environment. Our body has specific genes that recognize these toxins and effectively remove them from the body. People who have inherited a deficiency in these genes are more susceptible to heavy metal and xenobiotic (pesticides or herbicides) toxicity. As a consequence, it is advisable for people with certain genetics to avoid heavy metal containing foods (such as clams and large sea fish), consider choosing organically grown produce and more natural products, and to increase their mineral intake to bind and remove accumulating heavy metals from the body. [161 - 166]

- **Free Radical Protection (GSTM1, GSTT1, GSTP1, SOD2)**

  Free radicals are created primarily as a byproduct of energy metabolism and 5% of the oxygen you inhale is converted to these small aggressive molecules. If unchecked, these molecules can damage proteins, DNA and cell walls through a chain reaction of electron stealing. An imbalance between the creation and neutralization of free radicals results in cellular damage known as oxidative stress, which is one of the factors that affects the aging process. Certain genes are responsible for the neutralization of free radicals. Some people have genetic traits that reduce their protection from free radicals. If your body's innate ability to neutralize free radicals is reduced, you can consume higher levels of antioxidants — such as vitamin C, vitamin E, CoQ10, and Alpha Lipoic Acid — to increase your body's ability to resist oxidative stress. [167 - ]

  (continued on the next page)
- **Homocysteine Regulation (MTHFR)**

  Similar to high cholesterol, elevated homocysteine is a risk factor for cardiovascular health and is associated with numerous conditions, including coronary disease, stroke, peripheral vascular disease (carotid artery and cerebrovascular atherosclerosis), venous thrombosis, renal disease, diabetes mellitus, and organ transplant. [62 & 8]

  The MTHFR gene is one of the most well-documented gene-nutrient interactions. This gene codes for methylenetetrahydrofolate reductase which is an enzyme involved in folate metabolism and is involved in a process that carefully regulates the amount of homocysteine in the bloodstream. This process utilizes adequate intakes of folic acid (vitamin B9), vitamin B6, and vitamin B12. Some individuals have inherited genetic variations in the MTHFR gene that disrupts this protective function and can result in elevated homocysteine levels, especially if there is a dietary deficiency of folic acid [19]. In this case, utilization of pre-activated folate, called methyl folate or 5-MTHF, bypasses the inefficient MTHFR gene product and can establish optimal folate status, typically leading to reductions in homocysteine. Additionally, these individuals can further compensate with increased intakes of vitamins B6 and B12. [47 - 62]

- **Brain Health (APOE)**

  Understanding your genes can help you to understand the structural and metabolic traits of your brain. This knowledge helps to inform a program to support your brain health in an effective manner. For certain genotypes (specifically APOA4 homo- and heterozygotes), targeted nutrient intake may help mitigate genetic predisposition to accelerated health deterioration. [86 - 94]

- **Heart Health (APOA1, APOAS, APOB, CDH13, CHDS8, NOS3, PON1, MTRR, MMP3, GJA4, ITGB3, CETP, MTHFR, NOS1AP, AGT, ADRB1, GNB3)**

  There are many factors that affect the health of your heart and greater vascular system, including your genetics. Certain genetic variations may lead to nutrient deficiencies, but targeted dietary or supplemental support can meet your unique cardiovascular needs. For example, genetic variations are well documented to influence homocysteine levels, cholesterol levels in response to dietary components, QT interval, and blood pressure. Vitamins B6, B9, and B12, along with magnesium, CoQ10, and phytosterols have applications to mitigate the impact of specific gene variants associated with increased cardiovascular risk. [95 - 144]

- **Eye Health (HTRA1, CFH, ARMS2)**

  There are many genes that contribute to maintaining a healthy vision and common genetic variations can lead to certain deficiencies in this area. Gene screening can
inform increased risk of photodamage and structural degradation, and this information can be used to adjust nutrient intakes to maximize eye health. [145 - 152]

- Joint Health (TNFa, IL1a)

There are many genes that contribute to maintaining healthy joints and common genetic variations can lead to certain deficiencies in this area. By determining genetic strengths and weakness in regards to joint function, one can proactively adjust nutrient intakes to compensate with the correct nutrients with the aim to maintain mobility, and prevent joint discomfort and reduce the risk for catastrophic injury (fall in the elderly). [153 - 156]

Commitment to Science and Data

Though the field of genetic science is constantly evolving, Rootine commits to continuously reviewing new research and updating and refining our approach to product development accordingly.

Note

This whitepaper explores Rootine’s knowledge base and approach to product development as of the date of publication. The field of genetic science is continuously evolving and as such, findings may become outdated or change as new research emerges.

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