

How to Personalize Your Nutrition Based On Your Genes

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Disclaimer: *The information provided in this report is based on published SNP data and is for educational purposes only. It is important to understand that most published studies about DNA polymorphisms explain only a small part of the heritability of a trait or disease risk, and they also don't take into account how different polymorphisms may interact. In addition, many published studies do not account for environmental, dietary, microbial, medical history and lifestyle factors, which may all of the true risk for any trait or disease. You are strongly encouraged to discuss any genetic data with a doctor, genetic counselor or other health-care provider prior to making any medical decisions.*

There are a couple of consumer-available tools that allow you to understand how nutrients interact with your own genes, otherwise known as nutrigenomics, and how this affects metabolism and aging in general. We will also discuss a few examples of gene polymorphisms that you can readily be genotyped for that interact with nutrients, including: *MTHFR*, *NBPF3*, *FUT2*, *BCMO1*, *FADS1*, *FADS2*, *CYP2R1*, *PEMT*, *APOE*, and *FOXO3*.

23andMe

The first step in the process to finding out about whether you have these genes is a relatively inexpensive \$99 [23andMe test](#). 23andMe is a company that will test for common gene polymorphisms, which are variations in the DNA sequence of genes that can alter the function of that gene in a good way or a bad way. 23andMe no longer have health reports; however, they do provide the raw data, and that's still very useful.

Promethease

The second step is cheap tool called [promethease](#), costing only \$5. Promethease will match your raw data with a very large database, called SNPedia, which consists of over 57,000 published gene polymorphisms. Next, it generates a report with information about a person's attributes, such as propensity to diseases, based on the presence of specific SNPs within their genome. You will receive an email about 20 minutes later allowing you to view the results. You can arrange the results by magnitude and look at good and bad disease risks.

NOTE: All of the genotypes in this report are consistent with published scientific literature, SNPedia, and Promethease. This page explains why what the raw 23andMe data reporting is off for a some SNPs. It has to do with the orientation of the gene.

<http://www.snpedia.com/index.php/Orientation>.

Overview of Basics of Genetics

Gene polymorphisms are variations in the DNA sequence of genes that can alter the function of that gene in a good way or a bad way. Gene polymorphisms are different from mutations, which occur randomly on an individual basis, because polymorphisms are represented in some significant portion of the population, and might be presumed to have been "selected for." Polymorphisms make us members of a group and affect phenotype such as hair and eye color.

For every gene we have, we get one copy of it from mom and the other from dad, so we essentially have two copies of every gene. These copies are called alleles. In fact, if you were to look directly at the 23andme raw data it would become apparent that there are two letters

at every position in a gene. These are the DNA nucleotides that correspond to each of the two alleles-- one from mom and the other from dad. In some cases if a person is heterozygous for an allele, meaning they have different types of copies from mom & dad, they may have none or very little evidence of a trait that might be very bad if they had two copies of the exact same polymorphism. If you have two copies of the exact same polymorphism from mom and dad this is called homozygous (**Figure 1**). In other cases, some polymorphisms can have a dominant effect (even if you're only heterozygous), meaning having one copy of a specific polymorphism, the effect will still be significant enough to be measured. This is the case with having one polymorphism for brown eyes, which is enough to make the eye color brown.

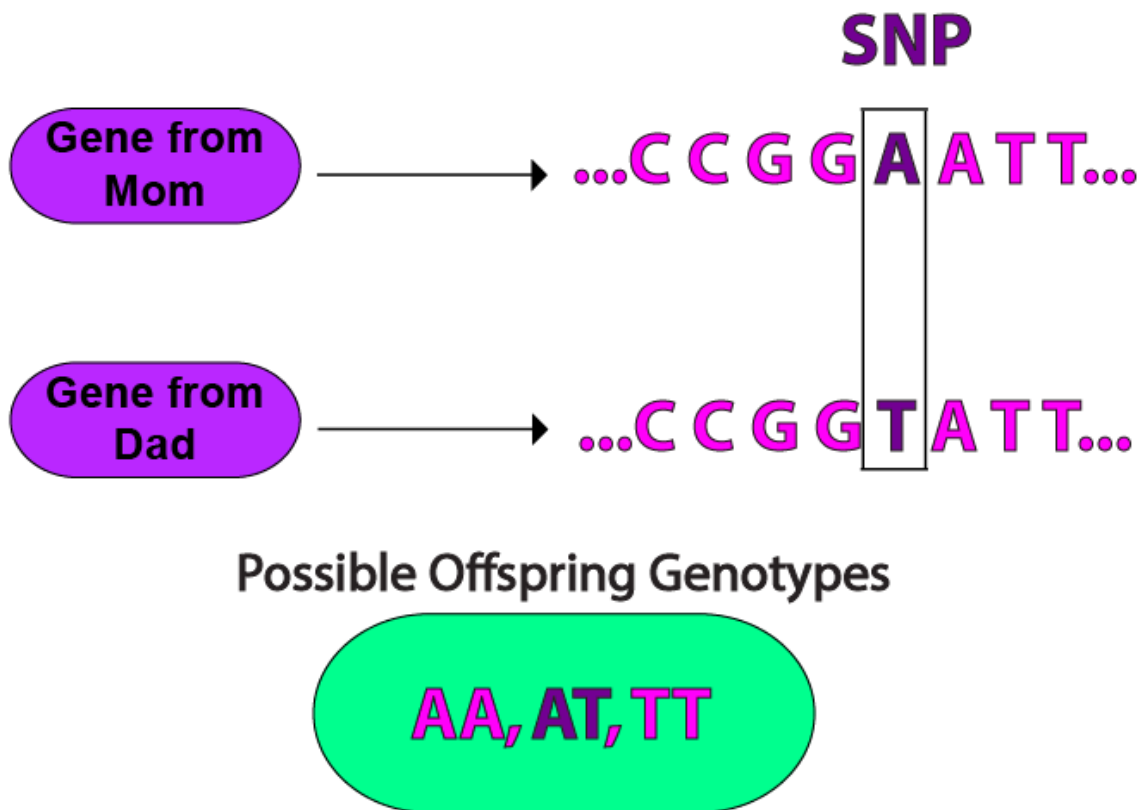


Figure 1: Single Nucleotide Polymorphisms (SNPs). A SNP is a change in one nucleotide DNA sequence in a gene. For every gene you have one allele from mom and one from dad. One of your parents may have a SNP that the other one does not, in which case the offspring would be heterozygous for that polymorphism. If both parents have same polymorphism then the offspring would be homozygous for this polymorphism.

Common Gene Polymorphisms Affecting Micronutrient Levels

It makes sense that varying ethnic populations have different versions of genes. Humans around the world share much in common but there are also many differences including: type of food availability, micronutrients in soil, accessibility to the ocean, viral and bacterial exposure, and distance from the equator. We likely have different versions of genes to help us cope with these environmental differences, many of which have to do with nutrients. Sometimes these different versions of genes come with a trade-off, particularly if we no longer live in the environment that selected for those genes.

In this report we will cover some very common gene polymorphisms in the population that affect how particular micronutrients are absorbed and metabolized including:

- Folate metabolism into precursors for methyl groups, which are used to lower homocysteine and for epigenetics.
- Vitamin B12 absorption in the gut.
- Vitamin B6 plasma levels.
- Conversion of beta-carotene into vitamin A.
- Conversion of the plant omega-3 fatty acid alpha linolenic acid (ALA) into the marine omega-3 fatty acid eicosapentaenoic acid (EPA).
- Production of phosphatidylcholine in the liver.
- Conversion of vitamin D3 into the active steroid hormone.

Folate and *MTHFR*

Folate (vitamin B9) serves two very important functions: 1). It serves as a precursor to make the DNA nucleotide thymine, which means it is essential to many new cells in the body, whether we are talking about the gut or the brain. 2). It serves as a precursor to make methyl groups, which are molecules that play a very important role in epigenetics. These methyl groups also play a very important role in converting homocysteine back into the amino acid methionine, which requires vitamin B12 as a cofactor.

There are a cluster of polymorphisms in the folate metabolism pathway. These specific polymorphisms are in the gene 5,10-methylenetetrahydrofolate reductase, known as *MTHFR*, which converts 5,10-methylenetetrahydrofolate into 5-methylfolate and uses riboflavin as a cofactor (**Figure 2**). 5-methylfolate is needed to make those methyl molecules that regulate

epigenetics and to convert homocysteine into methionine. This means that while people with *MTHFR* polymorphisms can make new DNA from dietary folate (or supplemental folic acid), they do not efficiently produce methyl groups and subsequently can have higher than normal homocysteine levels. High homocysteine is associated with a host of vascular diseases including coronary artery disease, stroke, and dementia.

While this cluster of polymorphisms effects a pretty large number of people, studies have shown that supplementing with L-5-MTHF (also known as 5-methylfolate), methylcobalamin (vitamin B12), and riboflavin are able to circumvent these shortcomings, and bring down homocysteine in these populations. For example, individuals homozygous for *MTHFR* (rs1801133 (T;T)) that supplemented with 480 micrograms of L-methyltetrahydrofolate for 4 weeks lowered their homocysteine levels by 15%. [Reference 1](#), [Reference 2](#)

The following are the cluster of polymorphisms and their corresponding loss of function:

- rs1801133 (C;T or T;C)
~40% of the population are heterozygous for one polymorphism which results in a 40% decrease in functional efficiency of *MTHFR*.
- rs1801133 (C;T or T;C) and rs1801131 (A;C or or C;A or C;C)
~20% of the population has two separate polymorphisms in the *MTHFR* gene which results in a 70% decrease in functional efficiency of *MTHFR*.
- rs1801133 (T;T)
~10% are homozygous for one polymorphism which results in 80-90% reduced functional efficiency of *MTHFR*. [Reference](#)

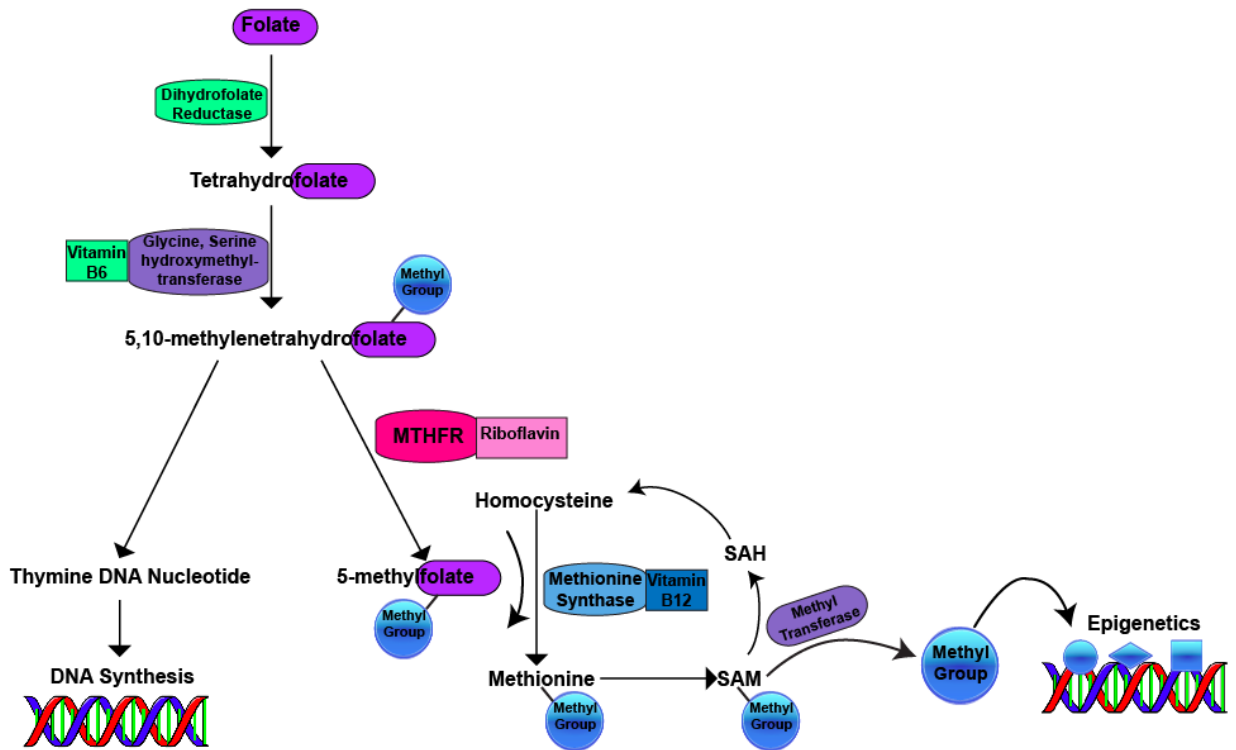


Figure 2: Folate Metabolism Pathways. Folate is converted into tetrahydrofolate via the dihydrofolate reductase enzyme. Tetrahydrofolate is converted into 5,10-methylenetetrahydrofolate via the vitamin B-6-dependent glycine, serine-hydroxymethyltransferase enzyme. 5,10-methylenetetrahydrofolate is required for two important pathways: **1).** The synthesis of nucleic acids (thymine) required to make new DNA. **2).** The production of 5-methylfolate by the riboflavin-dependent methylenetetrahydrofolate reductase (MTHFR) enzyme. The methyl group from 5-methylfolate is used to convert homocysteine into the essential amino acid methionine (via methylation) by the vitamin B12-dependent methionine synthase enzyme. Methionine, is now methylated in the form of S-adenosylmethionine (SAM) and this is used as a methyl donor via methyl transferase enzymes for a broad range of methylation reactions involved in epigenetics (DNA methylation). Once the methyl group is used from SAM, the methionine forms homocysteine again and the cycle starts over.

Vitamin B6 and *NBPF3*

There is a common polymorphism in the *NBPF3* gene that results in a decreased plasma vitamin B6 concentration. [Reference](#)

The following polymorphisms are associated with the the *NBPF3* gene:

- rs4654748 (C;T)

Approximately 46% of the population is heterozygous for this polymorphism resulting in 1.45 ng/ml lower plasma levels of vitamin B6 than normal.

- rs4654748 (C;C)
Some individuals may be homozygous for this polymorphism resulting in 2.90 ng/ml lower vitamin B6 levels.

Vitamin B12 and *FUT2*

There are very common variations in the *FUT2* gene that either decrease or increase vitamin B12 absorption. In those cases where poor vitamin B12 absorption occurs, sublingual vitamin B12 has been shown to bypass the malabsorption issue. [Reference](#)

The following are the cluster of polymorphisms and their corresponding functions:

- rs602662 (A;G or G;G)
Approximately 49% of the population is heterozygous for a polymorphism (A;G) that results in ~15% lower plasma vitamin B12 levels than normal. The same effect is observed in homozygotes (G;G). This effect is due to the polymorphism causing vitamin B12 malabsorption. [Reference](#)
- rs492602 (C;C)
Conversely, ~30% of population has a polymorphism in this gene that results in ~1.5 times higher plasma levels of vitamin B12 rs492602 (C;C) than normal. [Reference](#)

Vitamin A and *BCMO1*

There is large genetic variability in the metabolism of β -carotene into retinal, the pro-vitamin A. Provitamin A carotenoids are readily converted to vitamin A by *BCMO1* expressed in enterocytes of the intestinal mucosa. There are a cluster of polymorphisms in the *BCMO1* gene expressed in enterocytes of the gut. One polymorphism occurs in 42% and the other 24%. These SNPs reduce the ability of beta carotene to be converted into retinal (which is one of the many forms of vitamin A by between 30 to 70%. Foods of animal origin have the active form of vitamin A and supplements with active vitamin A can also be taken but be careful not to take too much as too much vitamin A can be toxic. [Reference 1](#), [Reference 2](#)

The following are the cluster of polymorphisms and their corresponding loss of function:

- rs7501331(C;T or T;T)
Approximately 24% of the population is heterozygous (C;T) for this polymorphism 5% of the population are homozygous (T;T)
- rs12934922 (A;T)
Approximately 42% of the population is heterozygous (A;T) and 22% of the population are homozygous (T;T).
- rs7501331 and rs12934922

Individuals that have one T in both SNPs have approximately 69% lower ability to convert Beta-carotene into pro-vitamin A.

Note: There are other polymorphisms in this gene that interact with each other and can affect efficiency broadly. Including: rs656485, rs6420424, rs11645428, and rs8044334.

Omega-3 Fatty Acids and *FADS2*

There are common polymorphisms in the delta desaturase genes (*FADS*) that elongate polyunsaturated fatty acids like alpha-linolenic acid (ALA) and convert it into eicosapentenoic acid (EPA). There are polymorphisms that decrease and increase this conversion. Since ALA is found in plants and EPA is found in fish, having one of these polymorphisms may influence how much fish you should consume. This polymorphism may also be particularly relevant to vegetarians, since many may mostly rely on ALA (from flaxseed or chia seed) as their source of EPA and DHA. If you're vegetarian, one other thing you might consider looking into is microalgae oil since it has EPA & DHA without having to be converted from ALA. [Reference](#)

The following are the polymorphisms that either decrease or increase the conversion of ALA to EPA:

- rs1535 (G;G)
This genotype is a "low converter" with ~29% poorer conversion of ALA into EPA relative to the high conversion genotype (A;A).
- rs1535 (A;G)
This genotype is a "intermediate converter" and has been associated with 18.6% poorer conversion of ALA into EPA relative to the high conversion genotype (A;A).
- rs1535 (A;A)
This genotype has been associated with the highest conversion of ALA into EPA.

Arachidonic Acid and *FADS1*

There are also common polymorphisms in another one of the *FADS* gene (*FADS1*) that affect levels of the inflammatory mediator arachidonic acid, making it higher or lower than normal. [Reference](#)

The following are the polymorphisms are associated with arachidonic acid levels:

- rs174537 (G;G)
This polymorphism has been associated with high arachidonic acid levels.
- rs174537 (G;T)
This polymorphism has been associated with intermediate arachidonic acid levels.
- rs174537 (T;T)
This polymorphism has been associated with low arachidonic acid levels.

Phosphatidylcholine/Choline and *FADS1*

There is another region in the *FADS1* gene that affects phosphatidylcholine levels. Phosphatidylcholine is a key component in all cell membranes and plays a very important role in the structure of the cell, which affects all biological functions. It is also a precursor for the neurotransmitter acetylcholine. [Reference](#)

The following are the polymorphisms associated with phosphatidylcholine levels:

- rs174548 (C;C)
This polymorphism has been associated with high phosphatidylcholine levels.
- rs174548 (C;G)
This polymorphism has been associated with intermediate phosphatidylcholine levels.
- rs174548 (G;G)
This polymorphism has been associated with low phosphatidylcholine levels.

Phosphatidylcholine/Choline and *PEMT*

Phosphatidylethanolamine-N-methyltransferase (*PEMT*) catalyzes the synthesis of phosphatidylcholine and, thus, choline in the liver. In addition to the important role phosphatidylcholine plays in cell membranes (particularly in neurons), it also is important in the liver. Phosphatidylcholine is required for the liver to secrete triglycerides into very low density lipoproteins (VLDL cholesterol). Decreased phosphatidylcholine can lead to decreased fat removal from the liver and, consequently, fatty liver. [Reference](#)

The following polymorphism is associated with reduced liver phosphatidylcholine production:

- rs7946 (A or A;A)
Having one A is associated with reduced *PEMT* function and is more pronounced if homozygous (A;A).

There is another common polymorphism in the *PEMT* gene; however, this specific polymorphism is not genotyped by 23andMe. *PEMT* is activated by estrogen but 44% of women have a polymorphism that makes *PEMT* unresponsive to estrogen. Remember, since *PEMT* makes phosphatidylcholine this means that premenopausal women are somewhat protected from low phosphatidylcholine due to low dietary intake. Postmenopausal women must increase their dietary intake of choline or phosphatidylcholine. For the 44% of women that have this polymorphism, the gene is unable to respond to estrogen, and thus, require a much higher dietary intake of choline or phosphatidylcholine. [Reference](#)

The following is the non-estrogen responsive polymorphism in the *PEMT* gene:

- rs12325817 (C;G or C;C)

Vitamin D and CYP2R1

There are two common polymorphisms in the *CYP2R1* gene (vitamin D 25-hydroxylase) that converts vitamin D3 into 25-hydroxyvitamin D, the major circulating form of vitamin D that gets converted into the active steroid hormone. This polymorphism can lower the conversion of D3 into 25-hydroxyvitamin D and, thus, is associated with lower circulating levels of 25-OHD and this has been associated with reduced longevity and higher all-cause mortality. It is known that supplementing with 1,000 IU of vitamin D3 per day generally raises serum 25-hydroxy levels by 5ng/ml. This may not be the case for people with these polymorphisms, and may require higher vitamin D supplementation doses to achieve the same serum levels as individuals without these polymorphisms. [Reference 1](#), [Reference 2](#), [Reference 3](#)

The following polymorphisms are associated with reduced CYP2R1 activity and low 25-hydroxyvitamin levels:

- rs10741657 (G;G)
- rs12794714 (A;A)
- rs2060793 (A;A)

APOE4

There are four different variations of the *apoE* gene that encodes for the lipoprotein that is made in the liver, where it binds to cholesterol and recycles it back to the liver. It is also made in astrocytes in the brain, where it transports cholesterol to neurons. Approximately 25% of the population has one allele (called *apoE4*) that does not recycle LDL very well and subsequently results in higher LDL in the bloodstream. In addition, it is associated with a 2 to 3-fold increased risk for Alzheimer's disease for multiple reasons. People with two alleles of the *ApoE4* gene fare even worse. I am currently researching ApoE biology in the brain and in the vascular system and writing a paper for publication. I will be covering this topic in depth in a future video/article. [Reference](#)

One *ApoE4* allele is associated with the following two separate polymorphisms:

- rs429358 (C;T) and rs7412 (C;C)

Two *ApoE4* alleles are associated with the following two separate polymorphisms:

- rs429358 (C;C) and rs7412 (C;C)

FOXO3

The *foxo3* gene is associated with longevity for several reasons. In flies and worms making more of this gene all of the time, it can extend their lifespan by 100%: a worm that would've only lived 15 days would instead live to ~30 days. In mice, having more of this gene can extend their lifespan by 30% and humans with a polymorphism that makes more of *foxo3* is associated with being a centenarian (that is, living to be at least 100 years old). The reason why having more *foxo3* is associated with longevity is because it turns on a whole host of genes that are involved in stress resistance making you more resilient to the damage that occurs everyday from just living (including normal metabolism and immune function). It turns

on many different antioxidant genes, DNA repair genes that repair damage to your DNA, genes that kill cancer cells, genes that prevent proteins from aggregating, and more. FOXO3 is awesome. [Reference](#)

The following polymorphisms are associated with the *foxo3* gene:

- rs2802292 (G;G)
This polymorphism is associated with between 1.5 to 2.7 times increased likelihood of living to be a centenarian.
- rs2802292 (G;T)
This polymorphism is associated with between 1.5 to 2 times increased likelihood of living to be a centenarian.

In summary, I think knowing what gene variations you have is a very useful tool that can be used to tailor your diet and lifestyle to your own genes such that you can find the optimal micronutrient and macronutrient intake in order to extend your lifespan and lower disease risk.