The Ultimate MTHFR Guide

The Most Studied Gene in Genomics

SelfDecode™

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MTHFR - The Most Studied Gene in Genomics

MTHFR is the most talked-about gene among health enthusiasts and functional medicine practitioners. It's also the best-studied gene in nutrigenetics, the science of how genes affect nutritional status.

MTHFR became such a popular topic after large-scale studies linked poor methylation with chronic health problems like:

- cardiovascular and thromboembolic diseases (specifically blood clots, stroke, embolism, and heart attacks)
- depression
- anxiety
- bipolar disorder
- schizophrenia
- colon cancer
- acute leukemia
- chronic pain and fatigue
- nerve pain
- migraines
- recurrent miscarriages in women of child-bearing age
- pregnancies with neural tube defects, like spina bifida and anencephaly

Learning what MTHFR variant is **extremely important** as it allows you to determine how efficient your body is with the methylation cycle. By understanding this, you're able to implement lifestyle changes that can help with methylation and increase your quality of life.

You can get a comprehensive MTHFR DNA Wellness Report with SelfDecode and get an in-depth, detailed explanation of your MTHFR gene, whether you carry the genetic mutation, and what you can do to optimize methylation.

Want to know exactly why the MTHFR is that important? Keep reading below to find out.

Part 1: What Is Methylation?

Methylation in humans affects the cytosine (C) nucleotide. It is the process by which a methyl group (a carbon atom with 3 hydrogen atoms attached to it) is bound to the cytosine nucleotides [R].

MTHFR, the most widely-studied gene in nutrigenomics is a key player in this process. People with two copies of the C677T variant (only 4% of the population) produce an enzyme whose activity is reduced by about 70% [R].
The steps to converting folate to MTHF or methyltetrahydrofolate involves many enzymes, including MTHFR.

- The methylation cycle starts with homocysteine.
- One of the molecules affected in this pathway is involved in making DNA.
- Another one, MTR or methionine synthase, converts homocysteine to methionine. It needs vitamin B12 and 5-MTHF to function.
- SAM-e has a methyl group attached to it, which it can "pass" to our DNA, causing DNA methylation.
- The end result of the methylation cycle is methionine, but it also produces other compounds important for antioxidant defense such as glutathione and affects folate metabolism.

We often hear about ways to turn "on" or "off" genes, but not about the biochemical basis on it is methylation: adding a methyl group is one way of turning on and off a gene. In normal cells, methylation ensures proper gene activation and silencing. DNA methylation causes a crucial modification to the genome that is involved in regulating many cellular processes. These processes include chromosome structure and stability, DNA transcription, and embryonic development [R,R].

But if the methylation cycle is less efficient – like if the activity of MTHFR is reduced – homocysteine can build up because not enough of it is being converted to methionine. High homocysteine levels are a big risk factor for many diseases – from inflammation and heart disease to diabetes, autoimmune diseases (like psoriasis), neurological issues, cancer, and others [R].

Types of Methylation

Methylation is the basis of epigenetics, the study of how the environment affects our genes. Our environment, lifestyle, and diet are all factors that can turn genes on or off. The patterns of methylation and demethylation presented here can have an impact on health, aging, and chronic diseases like cancer [R].
Although over- and under-methylation can both be harmful, it's important to consider which genes are being turned "on" or "off". Activating or deactivating some key regions can have the most serious health complications (such as hypomethylation of the so-called repeat sequences in cancer) [R].

1) DNA Hypermethylation

A healthy body has a certain level of methylation. Irregular and over-methylated DNA can change a gene, preventing it from producing what it's meant to. Changes in the placement of methyl groups can cause diseases [R].
Some researchers have even used the amount of methylation in certain genes as a biological clock, as its occurrence in individual genes is proportional to age. The implications include, but are not limited to:

- Causing cancer
- Lowering immune system function
- Damaging brain health
- Lowering energy and exercise
- Quickening aging

It can inactivate and reduce the expression of certain tumor-suppressor genes [R].

Additionally, external, environmental factors can alter methylation. In other words, while abnormal methylation in DNA can replicate itself and be passed down, this balance can also be altered by everything around us [R].

2) DNA Hypomethylation

Too little methylation can also be harmful.

If there is insufficient methylation in the body, it can cause genomic instability and cell transformation [R].

And although hypermethylation was thought to be more common in cancers, more recent research has revealed that hypomethylation also plays a role in these conditions. Hypomethylation can be beneficial for cancer short-term, but it may also speed up cancer growth [R].

Methylation in cancer has been described as “too much, but too little“. In cancer, some parts of the DNA are overmethylated, and other parts undermethylated, leading to a complete imbalance of the normal methylation cycle [R].

And aside from cancer, hypomethylation may also contribute to inflammation, leading to atherosclerosis and autoimmune diseases such as lupus and multiple sclerosis [R].

3) DNA Demethylation

DNA demethylation can also play a role in the formation of tumors [R].

But during embryo development, this process is crucial. Scientists have long struggled to understand how complex biochemical messages are communicated in the embryo to enable identical stem cells to develop into specialized cells, tissues, and organs. Demethylation happens in early embryos and is essential for stem cells to differentiate into specific cell types. DNA regions are turned on or off, and then modified via demethylation again for healthy development to take place [R].

Demethylation removes the modification of DNA nucleotides [R].

Part 2: What is Homocysteine?

Homocysteine is a sulfur-containing amino acid that the body produces from another amino acid, called methionine. Foods that are high in methionine include meat, egg whites, and seafood.

Homocysteine is usually found in very small amounts in your body. That's because your body converts it efficiently into other products with the aid of B vitamins. Higher homocysteine levels can indicate a deficiency of these vitamins [R].

Apart from vitamin deficiency, higher homocysteine levels have been linked to heart disease, cognitive dysfunction, and dementia.

The Breakdown of Homocysteine

Homocysteine is converted into less toxic and more useful amino acids via two biochemical pathways, i.e. remethylation or transsulfuration:

- Remethylation – A methyl group from 5-MTHF, a breakdown product of dietary folate, or betaine is added to homocysteine to convert it back to methionine. Vitamin B12 is needed in this process, as are the enzymes methionine synthase MTHFR [R, R].
- Transsulfuration – Homocysteine is converted to cystathionine by cystathionine β-synthase. Vitamin B6 is needed for this conversion [R,R]. Cystathionine can then be converted into cysteine and subsequently glutathione (a very powerful antioxidant) [R].

When homocysteine can not be converted to other compounds, it builds up in the body and may cause damage. B vitamins play a very important role in this balance.

Part 3: High Homocysteine Levels

Factors That Increase Homocysteine Levels

Causes listed below are commonly associated with elevated homocysteine. Work with your doctor or another health care professional to get an accurate diagnosis.

1) Genetics

Elevations in homocysteine can be caused by relatively common mutations in the MTHFR gene [R, R, R].

Every individual has 2 MTHFR alleles (1 from each parent). Mutation in just one MTHFR alleles is referred to as “heterozygous”; mutations of both is called “homozygous”. Approximately 10% of people of European descent have two mutations in this gene (homozygous form).

The two most common MTHFR mutations (polymorphisms) found in humans are:

- MTHFR C677T (Rs1801133). This mutation (the A allele) is associated with reduced enzyme activity, elevated total homocysteine levels and altered distribution of folate [R]. People with one “A” allele for this mutation have a 35% lower and people with “AA” genotype 68% lower enzyme activity [R].
- MTHFR A1298C (rs1801131). This mutation also impacts the MTHFR activity and homocysteine levels but to a lesser extent than C677T [R].

In a study of 872 healthy people, those who were homozygous for the MTHFR mutation (MTHFR 677TT genotype) were 10 times more likely to have high homocysteine levels compared to those with normal MTHFR [R].

Other genes that can impact homocysteine levels are genes that encode methionine synthase (MTR; rs1805087) and cystathionine-β-synthase (CBS; rs5742905, rs121964962) [R].

The MTHFR DNA Wellness Report analyzes your MTHFR gene and provides you with the genetic variant **you carry.** After that, you are given **PERSONALIZED** diet, lifestyle, and supplement recommendations that will help you either counteract the negative effect if you carry the risk variant, or boost the positive effects if you carry the good variant.

MTHFR-related SNPs

SNP	Your Genotype	Associations	Reference
rs1801131	TT	Normal MTHFR enzyme activity	9
rs1801133	AA	Significantly reduced MTHFR enzyme activity	94

Example SNP summary from MTHFR DNA Wellness Report

You can get your MTHFR DNA Wellness Report by signing up to SelfDecode here.

2) B Vitamin Deficiency

Homocysteine levels increase if there is:

- Vitamin B12 deficiency [R, R]
- Vitamin B6 deficiency [R]
- Folate (vitamin B9) deficiency [R, R]

Several studies that looked at people with different dietary patterns, found that people who were on a vegetarian or a vegan diet had significantly higher homocysteine levels, likely due to lower vitamin B12 levels [R, R, R, R].

Your genes can also tell you how well your body absorbs and retains vitamins like Vitamin B12 and Vitamin B6.

We want you to completely optimize your health and get the **complete** picture of your health, and MTHFR is only **one part** of it.

Our Vitamins DNA Wellness Report analyzes over 20 genes and lets you know how well your body absorbs certain vitamins. This can be extremely beneficial, especially if you have the mutation for MTHFR that causes undermethylation. For example, if you see that your gene puts you more at risk for Vitamin B12 deficiency, you'll know that you have to increase your B12 consumption.

Get the full picture of your health and start your journey to a healthier life here.

3) Stress

Several studies suggest that stress may increase homocysteine levels [R, R, R]. Mood issues like stress, anxiety, and depression are also implicated in a large amount of health problems like:

- Heart disease
- Asthma
- Obesity
- Diabetes

Solving your mood problems is a big step in reducing homocysteine, improving methylation, and optimizing your health altogether.

We've got the Mood DNA Wellness Report that can help you do all that!
Want a list of natural, **personalized** suggestions that can help you optimize your mood, methylation and your overall health in general?

Click here to get started!

4) Hypothyroidism

Several studies have found higher homocysteine levels in hypothyroidism [R, R, R]. A meta-analysis of 17 studies found that hypothyroid people not treated with levothyroxine had increased homocysteine levels, associated with the severity of hypothyroidism. Further, levothyroxine treatment was effective in reducing homocysteine levels [R].

Did you know that more than 12% of the U.S. population will develop a thyroid condition during their lifetime?

In fact, an estimated 20 million people in the U.S. currently have a thyroid disorder, and Levothyroxine (thyroid hormone) is the 2nd most prescribed drug in the country!

Genes play a significant role in determining whether or not you'll be a part of the 12% that develop thyroid issues.

There are 20 more genes that you can explore related to thyroid health that play critical roles in increasing your chances of having certain autoimmune diseases.

5) Smoking

Studies suggest that both smoking and exposure to second-hand smoke can increase homocysteine levels [R, R].

6) Alcohol

Daily alcohol consumption can increase homocysteine levels, likely by lowering vitamin B12 and folate levels [R, R].

7) Medication

Several drugs can increase homocysteine levels, including:

- Methotrexate, an immunosuppressant [R, R]
- Metformin, used in diabetes [R]
- Cholestyramine, used to lower cholesterol [R]
- Antiepileptics [R, R, R]

8) Kidney Disease

Kidneys help transform homocysteine into other amino acids [R]. Therefore, a decrease in kidney function can cause an accumulation of homocysteine.

9) Dental Health

Chronic periodontitis (inflammation of the teeth and gums) has been linked to elevated homocysteine levels in studies. This elevated homocysteine level returns to normal after the periodontal diseases are treated [R,R].

Part 4: Diseases Associated with High Homocysteine & What You Can Do

Elevated homocysteine levels have been linked to a number of diseases. However, if you have high homocysteine levels it doesn't mean you have any of the below-listed diseases!

High homocysteine levels are also encountered in:

- Sleep apnea [R]
- Autism [R, R]
- Gut disorders [R]

It is important to correct your homocysteine levels if possible. High homocysteine increases the risk of:

1. Heart Disease
2. Insulin Resistance
3. Depression
4. Cognitive Function, Dementia, and Alzheimer's Disease
5. Autoimmune Disease
6. Osteoporosis
7. Migraine

Get Your Personal MTHFR Gene Summary

If you want to know what version of the MTHFR gene you have and find out if it could be causing negative health effects, download your SelfDecode MTHFR DNA Wellness Report today.

You can upload your existing DNA file from a different company (like 23andMe, Ancestry and more), or you can get your genes tested for the first time with a Self-Decode DNA test kit.

Your SelfDecode reports won't just tell you what bad genes you have. They will provide personalized health recommendations so you can know exactly what supplement, diet and lifestyle changes to make in order to counteract any negative genetic variants you may have.


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