How to read your MTHFR gene testing results

What is the MTHFR gene and why is it important?

The MTHFR gene, short for methylenetetrahydrofolate reductase, is responsible for producing the MTHFR enzyme in the body. This enzyme regulates folate metabolism, a vitamin that is essential for new cell growth, production of new DNA and for our immune system. Another important role that the MTHFR enzyme plays is assisting the conversion of a molecule called homocysteine into methionine. Both folate and homocysteine metabolism are intricately linked, with low levels of the MTHFR enzyme causing simultaneous folate deficiency and high homocysteine levels (1). Folate deficiency puts a person at risk of a myriad of health problems including anemia (low red blood cell counts), pancytopenia (reduced red, white, and yellow blood cell counts) and cognitive changes (depression, irritability, fatigue) and infertility (2).

High homocysteine levels result in cardiovascular (affecting the heart and blood vessels), eye, neurological, developmental, and skeletal problems. Pregnant women may be more at risk of

preeclampsia (high blood pressure which can cause seizures), placental abruption (premature detachment of the placenta from the uterus), and recurrent pregnancy loss (3).

People with elevated homocysteine levels are also at risk of developing clots in the veins (known as thromboembolism) which may block blood flow in that vessel or break off, causing obstructions in other vessels (3). One common example of a thromboembolism is deep venous thromboembolism (DVT) which usually occurs in the legs. These blood clots may travel upwards into the lung, causing a pulmonary embolism which is a potentially life-threatening condition.

Why should we get tested for MTHFR gene mutations?

Mutations in the MTHFR gene have been thoroughly researched and are some of the most significant health modifiers in the human body. Depending on which type of polymorphism (mutation) you have, your body may have between 20 – 70% loss of function of the MTHFR enzyme.

The two most common MTHFR gene mutations are the C677T and A1298C mutations. In the Australian population, up to 8 – 20% of people are homozygous for the C677T, meaning that they have two copies of the mutated gene and only have 30% normal MTHFR enzyme activity (more on this below). The other A1298C mutation is found in 7 – 12% of the Australian population (3).

Breaking down the results

Before reading any report, please be sure to double check the personal details of the test results to confirm that the results are really yours.

1. Types of MTHFR mutations tested for

The two most common MTHFR mutations are the C677T and A1298C mutations – both of which are tested for with our test kit. If you are using another lab, please ask them to check both variants.

2. Heterozygous, homozygous, or wild type (means no mutation)?

All humans have two copies of each gene – one from mum and another from dad.

Heterozygous means that you have inherited one copy of the mutated gene from either mom or dad.

Homozygous means that you have inherited two copies of the mutated gene – one from mom and another from dad.

The table below shows several different combinations that may be reported on your test results, with an approximate percentage loss of enzyme activity.

A1298C Mutation	C677T Mutation	Loss of Enzyme Activity
Homozygous	-	40%
Heterozygous	-	20%
Heterozygous	Heterozygous	40 - 50%
-	Heterozygous	40%
-	Homozygous	70%

3. What do these results mean?

Being homozygous or heterozygous for an MTHFR gene mutation means something different for every person. ***It does not mean that you are sick***.

Having reduced MTHFR enzyme activity does not mean that a person will definitely have elevated homocysteine levels or low folate, however it may mean that you are more susceptible to low levels if you are affected by stress, bad diet, lack of sleep, lack of exercise and other environmental stressors like viruses, bacteria, and the like (3).

Let us look at some results and explain what they mean.

GENOMIC_ASSESSMENTS

SWAB, Buccal	Result	Range	Units

MTHFR Gene Mutation

MethyleneTetraHydroFolate Reductase (MTHFR) Gene Mutation.

MTHFR Gene Mutation (A1298C): HETEROZYGOUS for the mutation.
MTHFR Gene Mutation (C677T): Negative - Mutation not found.

These results indicate that the person has one copy of the A1298C polymorphism. So, either Mum or Dad gave you the copy. Your down regulation may be around 20%.

GENOMIC_ASSESSMENTS

SWAB, Buccal	Result	Range	Units

MTHFR Gene Mutation

MethyleneTetraHydroFolate Reductase (MTHFR) Gene Mutation.

MTHFR Gene Mutation (A1298C): HOMOZYGOUS for the mutation.
MTHFR Gene Mutation (C677T): Negative - Mutation not found.

This person is Homozygous A1298C. It means that both Mum and Dad gave them the polymorphism. This may cause a 40% reduction in enzyme activity which means they may be susceptible to anxiety and depression if they do not keep folate levels at a good level. Eating leafy green vegetables is key. With fertility, we would recommend having an assessment by one of our fertility practitioners to help you ascertain the best level of folate for you.

GENOMIC_ASSESSMENTS

SWAB, Buccal	Result	Range	Units

MTHFR Gene Mutation

MethyleneTetraHydroFolate Reductase (MTHFR) Gene Mutation.

MTHFR Gene Mutation (A1298C): HETEROZYGOUS for the mutation.
MTHFR Gene Mutation (C677T): HETEROZYGOUS for the mutation.

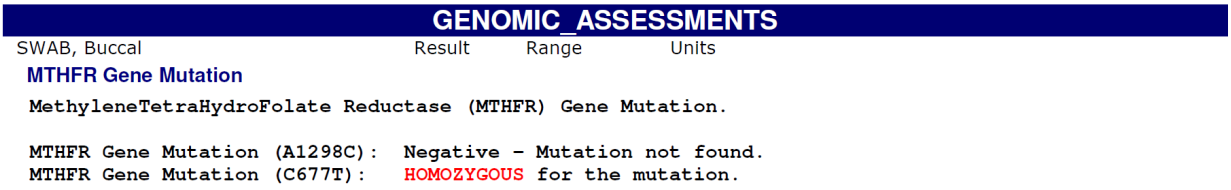
This person has one copy of each of the A1298C and the C677T polymorphisms. We call this ‘compound heterozygous’ and the reduction in enzyme activity may be as high as 50%.

MTHFR Gene Mutation, Bloodspot

MethyleneTetraHydroFolate Reductase (MTHFR) Gene Mutation.

MTHFR Gene Mutation (A1298C): Negative - Mutation not found.
MTHFR Gene Mutation (C677T): HETEROZYGOUS for the mutation.

This person is heterozygous for the C677T. This means they may have a 40% down regulation of the enzyme.



This person is homozygous for the C677T. This is the polymorphism which is most likely to affect health as the potential downregulation of the enzyme can be as high as 70%. It is important to evaluate environmental factors and stressors that may influence health.

If you have a report that says: homozygous Wild type - that means you have no polymorphisms.

The 'wild type' is what we expect to see in the normal DNA sequence.

4. What is quantitative real-time polymerase chain reaction (qRT-PCR)?

This is a laboratory method for detecting levels of genes in your samples. The same test is conducted on all samples taken.

What can I do if I am tested positive for an MTHFR mutation?

Having an MTHFR mutation means that you may need to take some extra steps to ensure that your overall health is supported during times of stress, sickness or infection. Below are several recommendations:

- Avoid cereal grains (because they are fortified with folic acid (not the right form of folate we want - see our Folic vs 5-MTHF article
- Avoid dairy products (they put extra stress on our immune system)
- Avoid processed foods (they lack nutrients and folic acid is usually added)
- Lower alcohol consumption (it depletes all our B Vitamins)
- Quit smoking (puts too many harmful chemicals into our body)
- Reduce/modulate stress (stress responses consume the most methyl groups. So, trying yoga, meditation, just walking in nature is important)

· Reduce environmental toxins (MTHFR mutations impair the ability to detoxify, placing extra stress on the liver). Just changing your personal care products and cleaning products can be important.

· Increase vegetable consumption (especially dark leafy greens as they provide natural folate your body can convert to methyl folate)

· Maintain a healthy weight.

References

1. Blom HJ, Smulders Y. Overview of homocysteine and folate metabolism. With special references to cardiovascular disease and neural tube defects. J Inherit Metab Dis. 2011;34(1):75-81.

2. Folic Acid Deficiency. [Updated 2020 Jun 30] [Internet]. Treasure Island (FL): StatPearls Publishing. 2021 [cited 3rd May 2021]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK535377/.

3. Moll S, Varga Elizabeth A. Homocysteine and MTHFR Mutations. Circulation. 2015;132(1): e6-e9.