G E N E M T H F R

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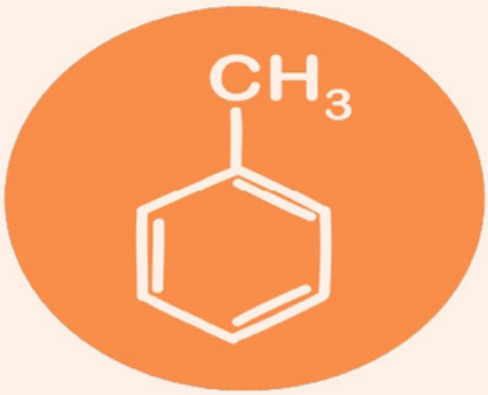
Your genetic guide to

METHYLATION REPORT



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Introduction

MTHFR (methylenetetrahydrofolate reductase) is an enzyme that adds a methyl group to folate to convert it into its active form. This enzyme maintains the cellular folate levels and is a cofactor which is required for the conversion of homocysteine (a harmful amino acid) to methionine. The MTHFR gene and other associated genes regulate the production and activity of the MTHFR enzyme.

Methyl-folate is important for methylation, the process in which a methyl group is added to a compound. This process is important in many of the biological processes in the body like

- **Repair and regeneration of cells, tissues and DNA**
- **Regulation of gene expression and also in protein function**
- **Synthesis of neurotransmitters which are associated with mood, behavior, sleep, cognitive ability and memory**
- **Maintain homocysteine levels**
- **Alteration of toxins and heavy metals that are potentially harmful**
- **Aiding the liver in the breakdown of fats**
- **lowering risk of inflammation**
- **Activation of the immune system**

Specific genetic variations in the MTHFR genes are associated with reduction in the function of the MTHFR enzyme, with nearly 30 to 70% reduction in methyl-folate when compared to people without the variations.

This reduction has been found to lead to increased levels of homocysteine, which in turn increases the risk for venous thrombosis and cardiovascular disease. Another significant effect of reduced MTHFR enzyme is its effect on folate status, subsequently affecting sensitivity to methotrexate drugs. These drugs are structural analogues to folate and are used in the treatment against many autoimmune disorders and for various types of cancer. Genetic variations that affect MTHFR enzyme function could, therefore, affect sensitivity to methotrexate drugs and lead to reduced dose requirement, or an increase in side effects.

Genetic variations in the MTHFR and associated genes are associated with

- **elevated homocysteine levels**
- **impaired methylation processes**
- **limited detoxification capacity**

This test could help individuals presenting with the following conditions-

* Coronary artery disease * Elevated homocysteine * Bipolar disorder * Schizophrenia * Peripheral vascular artery disease * Acute myocardial infarction * Depression * Stroke * Venous thromboembolism * Migraines * History of preeclampsia, neural tube defects, recurrent miscarriages * Autism spectrum disorders

An MTHFR status report is one of the many indicators for identifying the risk of developing cardiovascular disease, or the risk for neural tube defects and sensitivity to methotrexate. However, it is not predictive of disease development and should not be used as the primary means of clinical diagnosis or in therapy decision making. The information provided must be interpreted only by a qualified physician.

While genetic factors play a role in elevated homocysteine levels, other factors include a diet rich in methionine, chronic kidney disease and stress, amongst others.

This report profiles more than 70 known genetic polymorphisms in the MTHFR gene and related genes.

Introduction

Human health is a complex interplay between genetics and the environment (lifestyle, diet, activity, stress, etc.). Your genes and the environment that you are exposed to, both play a vital role in your overall health and well-being.

This report is presented in a user friendly language and format. The following tips will help you get the best information value out of the report.

1. What do "Normal" and "Risk" in the tables indicate?

NORMAL and RISK indicate the "Normal" and "Risk" version of the polymorphism, respectively. If your "GENO" has the Risk version, then its indicated by an orange or red color. GENO indicates your genotype.

2. What does rank mean?

Certain genes are found to have a higher impact and variations in these genes are more likely to have an adverse effect on Health, such genes are ranked higher than the others. So, greater the rank, higher the adverse impact of the gene.

3. Where did the information contained in the report come from?

The genetic markers that are used in this report are based on scientific studies published in international journals. A list of references is available for you to read on our web blog.

4. The word “likely” is used often in the report. What does it mean?

People generally know that high cholesterol can lead to heart conditions. However, there are individuals with high cholesterol who do not develop heart disease. Similarly, smoking can lead to lung disease, but not always. Hence, certain genetic parameters can lead to certain outcomes but other factors may modify the outcome. “Likely” means, it is more likely that one will see the outcome, but other factors may modify it.

5. What does the term “moderate” mean in the report?

Moderate implies neither high nor low, rather an intermediate outcome. For example, moderate enzyme activity is an intermediate level between low and normal enzyme activity.

PROMINENT MTHFR SNPS

RSID	GENO	ENYME ACTIVITY	RESPONSE TO METHOTREXATE
rs1801133	GG	Normal MTHFR enzyme activity	[illegible]
rs1801131	TT	Normal MTHFR enzyme activity	[illegible]

Your Result

NORMAL MTHFR ENZYME ACTIVITY

OTHER MTHFR SNPS

RSID	GENE	NORMAL	RISK	RANK	GENO
rs162031	MTRR	T	C	Low	CC
rs2236225	MTHFD1	G	A	High	AA
rs803422	MTHFD1L	A	G	Low	GG
rs11754661	MTHFD1L	G	A	Low	GG
rs17349743	MTHFD1L	T	C	Low	TC
rs2066470	MTHFR	G	C	Medium	GG
rs1801131	MTHFR	T	G	Medium	TT
rs17367504	MTHFR	A	G	Low	AA
rs3737964	CLCN6	T	C	Low	CC
rs13306560	CLCN6	C	T	High	CC
rs17037390	MTHFR	G	A	Medium	GG
rs4846048	MTHFR	G	A	Low	AA

rs1801133	MTHFR	G	A	High	GG
rs2274976	MTHFR	C	T	Medium	CC
rs1476413	MTHFR	C	T	Medium	CC
rs6495446	MTHFS	C	T	Low	TC
rs2733103	MTHFS	C	T	Low	CC
rs11799670	MTR	A	G	Low	AA
rs1805087	MTR	A	G	High	AG
rs10925257	MTR	A	G	Low	AG
rs2275568	MTR	C	T	Low	CC
rs3820571	MTR	G	T	Low	TG
rs2275565	MTR	G	T	Low	TG
rs1802059	MTRR	G	A	Low	AG
rs3776455	MTRR	C	T	Low	TT
rs1532268	MTRR	C	T	Low	TC

UNDERSTANDING YOUR REPORT

People who carry many high risk gene variations and who have high homocysteine levels have been associated with the following conditions. If you have a high genetic risk along with high homocysteine levels, watch out for symptoms and consult your physician about possible therapy.

Reference Range for Plasma Homocysteine Levels-

According to Centres for Disease Control (CDC)

[redacted]

Homocysteine level and associated conditions- The metabolism of methionine, an essential amino acid, produces homocysteine, which is converted back into methionine by remethylation. Abnormalities in this pathway lead to hyperhomocysteinemia- a condition characterized by high levels of Homocysteine in blood. Approximately, 5% of the general population suffers from hyperhomocysteinemia.

Neural Tube Defects- Neural tube defects are a failure of the neural tube of the growing fetus to close completely. Numerous studies have shown that high maternal homocysteine levels was associated with an elevated risk for neural tube defects among the offspring.

Congenital Heart Defects- Congenital Heart Defects develop during the first three weeks after conception, with an incidence of 11 per 1000 live births (US). A meta-analysis showed that maternal homocysteine was associated with a significant increase in congenital heart disease.

Cardiovascular Disease- Numerous studies have identified homocysteine as an independent risk factor for cardiovascular disease.

Down Syndrome- The risk for down syndrome was found to be elevated in the presence of the

Alzheimer's Disease- High homocysteine levels and low folate intake have been shown to be associated with poor cognitive performance. High levels of homocysteine is associated with neurotoxicity and vasotoxicity, leading to dementia and Alzheimer's disease.

Breast Cancer- Folate deficiency has been found to increase the risk for various cancers due to impaired DNA repair synthesis and disruption of DNA methylation which may result in proto-oncogene activation.

Depression- Hyperhomocysteinemia has been associated with impaired methylation reactions in the central nervous system, which is associated with depressive disorders.

RECOMMENDATIONS

Natural Ways to Lower Plasma Homocysteine Levels

Lowering plasma homocysteine levels is found to lower the risk for diseases. In a study conducted to identify the reduction in risk for various cardiac diseases, a reduction in 3 μmol/l of homocysteine from elevated levels was found to reduce the risk of deep vein thrombosis by 25% (8% to 38%), ischaemic heart disease by 16% (11% to 20%) and stroke by 24% (15% to 33%).

- **Vitamin B6 rich foods include a variety of protein foods, fish, turkey,eggs, poultry, legumes (beans and peas), nuts, seeds, and soy products.**
- **5-methyltetrahydrofolate- The MTHFR enzyme breaks down folic acid to 5-methyltetrahydrofolate (5-MTHF), which is the methyl group donor required for the remethylation of homocysteine to methionine. Supplementation with 5-MTHF has been shown, in many studies, to lower the levels of homocysteine.**

A scientific study conducted on the extent of reduction in homocysteine levels showed that 113mcg/day of 5-MTHF reduced plasma homocysteine levels by approximately 14.6% over a period of six months. 5-MTHF is found to raise blood folate levels by nearly 7 times when compared to ordinary folic acid .

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Only full genome sequences are exhaustive. All other forms of genetic tests only provide a limited subset of genetic information relevant to specific conditions. Since this report is not generated by conducting a whole genome sequence test, the results reported are limited to a specific set of mutations known to be associated with specific conditions. Genetic information is also subject to revision based on the latest advances in scientific research. Therefore the interpretation of results reported herein may vary or be altered subject to ongoing research. Sometimes, the interpretations may vary from company to company based on which studies are being given a higher preference compared to others.

Xcode's role is limited to providing genetic test results and a broad set of recommendations. More detailed recommendations that may be specific to you are to be made by qualified Professional Practitioners only. General guidelines provided in our report are for information purposes only and are meant to aid your Professional Practitioner in rendering the relevant professional or medical advice and treatment. While assessing your genetic parameters and providing the report and recommendations, we do not consider your past or existing health conditions and any medication you took (either in the past or currently), even if you may have provided us with such information. Our report and recommendations are to be acted upon in consultation with a medical or other health and wellness professional practitioner.

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