geneticgenie

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Gene & Variation	rsID	Alleles	Result
COMT V158M	rs4680	AA	+/+
COMT H62H	rs4633	TT	+/+
COMT P199P	rs769224	GG	-/-
VDR Bsm	rs1544410	CC	-/-
VDR Taq	rs731236	AA	+/+
MAO A R297R	rs6323	TT	+/+
ACAT1-02	rs3741049	GG	-/-
MTHFR C677T	rs1801133	GG	-/-
MTHFR 03 P39P	rs2066470	GG	-/-
MTHFR A1298C	rs1801131	GT	+/-
MTR A2756G	rs1805087	AA	-/-
MTRR A66G	rs1801394	AG	+/-
MTRR H595Y	not found	n/a	n/a
MTRR K350A	rs162036	AA	-/-
MTRR R415T	not found	n/a	n/a
MTRR A664A	rs1802059	AG	+/-
BHMT-02	rs567754	CC	-/-
BHMT-04	not found	n/a	n/a
BHMT-08	rs651852	CC	-/-
AHCY-01	rs819147	TT	-/-
AHCY-02	not found	n/a	n/a
AHCY-19	rs819171	TT	-/-
CBS C699T	rs234706	AA	+/+
CBS A360A	rs1801181	GG	-/-
CBS N212N	not found	n/a	n/a
SHMT1 C1420T	not found	n/a	n/a

Before getting started: Understanding the basics

We have two copies of most of the genes we are born with - one from our mother and one from our father. Genetic Genie uses the SNPs (Single Nucleotide Polymorphisms) generated from your unique DNA sequence to determine if one or both copies of your genes have a mutation at a specific location in a specific gene. If there are no mutations present, your result will be displayed as (-/-). If one gene is mutated, the result will read (+/-). If both copies have a mutation, the result is (+/+). Along with the (+/-) symbols, the colors on the table also denote the type of mutation for visual comprehension. The color red indicates a homozygous (+/+) mutation, the color yellow indicates a (+/-) heterozygous mutation and the color green (-/-) indicates that you don't carry the specific mutation.

The terms heterozygous and homozygous are used by geneticists to denote whether one or both copies of a gene are mutated. Heterozygous mutations (+/-) may differ from homozygous mutations (+/+) in associated disease risk since a person with a heterozygous mutation will often still have one fully functioning copy of the gene. It is also important to understand that having a gene with a SNP mutation does not mean that the gene is defective or nonfunctioning, only that it is working with an altered efficiency. Sometimes this means that it is working at a decreased level, but it could also mean that it is functioning at a higher than normal efficiency, or that the gene is lacking regulatory mechanisms normally involved in its expression.

Although mutations can occur at any time during our lifetime, it is most likely that we are born with these mutations and will have them throughout our life. These inherited mutations have been passed down to us from previous generations (our parents and grandparents) and may be passed to future generations (our children). This may provide an explanation as to why certain traits or diseases "run in the family".

Although we cannot change our genetic code, we can change how our genes are expressed. Research has revealed that our gene expression is not determined solely by hereditary factors, but it is also influenced by our diet, nutritional status, toxic load and environmental influences or stressors. This phenomenon has been termed "epigenetics". Researchers in the growing field of epigenetics have demonstrated that certain genes can be over- or under-expressed with certain disease processes. Researchers in this field hope that by understanding of how these genes are regulated and what is influencing them, we may be able to change their expression. Using epigenetic concepts along with a good understanding of the methylation cycle, researchers have begun to make recommendations to optimize genetic expression and help to restore health.

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MTHFR Mutations

First we'll look at a few of your MTHFR mutations. According to research, these mutations are important and can be implicated in various disease states.

You have 1 heterozygous (yellow) mutation(s). These are generally not as bad as red homozygous mutation, but they may still worth paying attention to. They include:

- MTHFR A1298C

Now let's move on to discuss what these MTHFR mutation(s) mean.

MTHFR A1298C

MTHFR A1298C is involved in converting 5-methylfolate (5MTHF) to tetrahydrofolate (THF). Unlike MTHFR C677T, the A1298C mutation does not lead to elevated homocysteine levels. This reaction helps generate BH4. BH4 is important for the detoxification of ammonia. The gene is compromised about 70% in MTHFR A1298C (+/+) individuals, and about 30% in people with a heterozygous (+/-) mutation.

BH4 acts as a rate limiting factor for the production of neurotransmitters and catecholamines including serotonin, melatonin, dopamine, norepinephrine, and epinephrine. A MTHFR A1298C + status may cause a decrease in any of these neurotransmitters or catecholamines. BH4 is also a cofactor in the production of nitric oxide. A dysfunctional BH4 enzyme may lead to mental/emotional and/or physical symptoms. Mercury, lead, and aluminum may act as a drain on BH4.

All of Your Other Mutations

Now we are going to look at all of your mutations. You do not necessarily need to worry about all of these mutations, but certain mutations may cause problems in certain individuals. Genetic Genie does not look at the expression of your genes, it only looks at specific gene SNPs. Keep in mind that even if you are homozygous or heterozygous for a certain mutations, it doesn't necessarily mean there is a problem with the functioning of that gene. You have 5 homozygous (+/+) mutations and 2 heterozygous (+/-) mutations.

Here are your homozygous mutations as indicated in your SNP gene table above (not including MTHFR):

- COMT V158M
- COMT H62H
- VDR Taq
- MAO-A R297R
- CBS C699T

Here are your heterozygous mutations as indicated in your SNP gene table above (not including MTHFR):

- MTRR A66G
- MTRR A664A

CBS Mutations

CBS (cystathionine beta synthase) catalyzes the first step of the transsulfuration pathway, from homocysteine to cystathionine. CBS defects are actually an upregulation of the CBS enzyme. This means the enzyme works too fast. In these patients, it's common to see low levels of cystathionine and homocysteine since there is a rapid conversion to taurine. This leads to high levels of taurine and ammonia. The CBS upregulation has been clinically observed to result in sulfur intolerance in some patients. It has also been observed that BH4 can also become depleted with a CBS upregulation. BH4 helps regulate neurotransmitters and mood. Other mutations, such as MTHFR A1298C, Chronic bacterial infections, and aluminum can also lead to low BH4 levels. Lack of BH4 can lead to mast cell degranulation and possibly mast cell activation disorder (MCAD).

Note: While some physicians think the CBS mutation is one of the most important mutations to address, there is very little medical research to support these claims and some doctors in the field disagree. In normal populations, studies have shown CBS upregulations to be protective against high homocysteine. However, CBS upregulations have shown to be harmful in Down Syndrome. Medical research has not determined if CBS upregulations are harmful in those with syndromes or disorders leading to impaired methylation.

MTR/MTRR Mutations

MTRR (Methionine synthase reductase) helps recycle B12. The combination of MTR and MTRR mutations can deplete methyl B12. MTR A2756G, MTRR A66G, MTRR H595Y, MTRR K350A, MTRR R415T, MTRR S257T, and MTRR A664A all work together to convert homocysteine to methionine.

MTR (5-methyltetrahydrofolate-homocysteine methyltransferase) provides instructions for making the enzyme methionine synthase. Methionine synthase helps convert the amino acid homocysteine to methionine. To work properly, methionine synthase requires B12 (specifically in the form of methylcobalamin). An MTR A2756G mutation increases the activity of the MTR gene causing a greater need for B12 since the enzyme causes B12 to deplete since it is using it up at a faster rate. Mutations in MTR have been identified as the underlying cause of methylcobalamin deficiency. Megaloblastic anemia can occur as a consequence of reduce methionine synthase activity.

A homozygous mutation of MTR A2756G is not very common (<1% of CEU population). Some studies have demonstrated that people with a combination of MTHFR C677T and MTR A2756G have persistently high homocysteine levels unless they are treated with both B12 and folate.

MAO-A R297R

MAO-A (Monoamine oxidase A) is a critical enzyme involved in breaking down important neurotransmitters such as serotonin, norepinephrine, and dopamine. Males only have one allele since the gene is inherited through from their mother since it is located on the X chromosome. Only females can be heterozygous (+/-) for this mutation. When a (+/+) MAO-A mutation is combined with a (+/+) or (+/-) COMT V158M mutation, imbalances in neurotransmitters may be more severe. These imbalances can potentially lead to neuropsychiatric conditions and symptoms such as Obsessive Compulsive Disorder (OCD), mood swings, and aggressive and/or violent behavior.

Note: Genetic Genie reports the wild type as the defective variant as doctors have clinically observed that patients with methylation problems (especially those of Autism) often have trouble breaking down neurotransmitters. The high activity version of MAO-A (which is represented as -/-) can contribute to major depressive disorder. The significance of this SNP should be interpreted with caution.

COMT Mutations

COMT (catechol-O-methyltransferase) helps break down certain neurotransmitters and catecholamines. These include dopamine, epinephrine, and norepinephrine. Catechol-O-methyltransferase is important to the areas of the pre-frontal cortex. This area of the brain is involved with personality, inhibition of behaviors, short-term memory, planning, abstract thinking, and emotion. COMT is also involved with metabolizing estrogens.

COMT (-/-) individuals can usually break down these neurotransmitters efficiently, but COMT (+/+) individuals may have trouble breaking these chemicals down from impaired function of the enzyme. With a COMT + status, it has been clinically observed by physicians that people may have trouble with methyl donors. This can lead to irritability, hyperactivity, or abnormal behavior. They may also be more sensitive to pain.

VDR Mutations

VDR (Vitamin D Receptor) encodes the nuclear hormone receptor for vitamin D3. Low or low normal vitamin D values are often seen in those with chronic illness and even the general population. Low vitamin D is related to a lot of neurological and immunological conditions. Vitamin D stimulates enzymes that create dopamine.

VDR Tak and VDR Bsm are usually inverse from eachother. So if there is a (+/+) VDR Tak, there would be a (-/-) VDR Bsm. However, this is not always the case.

It has been clinically observed that the body may have trouble tolerating methyl donors with a COMT V158M + and a VDR Taq + status. VDR Taq (-/-) individuals may already have higher levels of dopamine, and combinations of variations COMT and VDR Taq can lead to a wide range of dopamine levels. Those that are VDR Taq (+/+) and COMT (-/-) may have lowest dopamine levels.

Note: Some have pointed out that VDR Taq is reported backwards since majority of medical journals report a different risk allele or use different notation. These arguments are well-founded, but Genetic Genie reports this way so results are compatible with existing methylation nutrigenomics literature. Many claims about VDR and methylation are clinical observations. There are no medical studies to support some of the observations.

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