geneticgenie

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Gene & Variation	rsID	Alleles	Result
COMT V158M	rs4680	AG	+/-
COMT H62H	rs4633	CT	+/-
COMT P199P	rs769224	GG	-/-
VDR Bsm	rs1544410	TT	+/+
VDR Taq	rs731236	GG	-/-
MAO-A R297R	rs6323	TT	+/+
ACAT1-02	rs3741049	GG	-/-
MTHFR C677T	rs1801133	AG	+/-
MTHFR 03 P39P	rs2066470	GG	-/-
MTHFR A1298C	rs1801131	TT	-/-
MTR A2756G	rs1805087	AG	+/-
MTRR A66G	rs1801394	AG	+/-
MTRR H595Y	rs10380	__	no call
MTRR K350A	rs162036	AA	-/-
MTRR R415T	rs2287780	__	no call
MTRR A664A	rs1802059	AG	+/-
BHMT-02	rs567754	CT	+/-
BHMT-04	rs617219	__	no call
BHMT-08	rs651852	CT	+/-
AHCY-01	rs819147	CT	+/-
AHCY-02	rs819134	__	no call
AHCY-19	rs819171	CT	+/-
CBS C699T	rs234706	AA	+/+
CBS A360A	rs1801181	GG	-/-
CBS N212N	rs2298758	__	no call
SHMT1 C1420T	rs1979277	__	no call

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 C677T

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

MTHFR C677T

One function of MTHFR (Methylenetetrahydrofolate reductase) is to help convert homocysteine to methionine. A MTHFR C677T mutation means that the MTHFR enzyme may have trouble performing its task leading to high levels of homocysteine. According to Dr. Ben Lynch, impaired function of the enzyme can cause or contribute to conditions such as Autism, Chronic Fatigue Syndrome, Fibromyalgia, Miscarriages, IBS, many birth defects, Multiple Sclerosis, Alzheimer's, Bipolar Disorder, blood clots, Stroke, Chemical Sensitivity, and many other conditions.

MTHFR C677T can also lead to high homocysteine. High levels of homocysteine can be related to MTHFR C677T mutations. While homozygous (+/+) or heterozygous (+/-) mutations indicates reduced activity of this enzyme, it does not necessarily mean there will be high homocysteine levels in a clinical setting.

As S-adenosylhomocysteine (SAH) accumulates, the COMT enzyme may become impaired. Inhibitiion of COMT can increase dopamine levels in COMT V158M (-/-), but for those with COMT V158M (+/+), the high level of SAH can lead to behavior problems and mood swings according to Dr. Amy Yasko.

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 3 homozygous (+/+) mutations and 9 heterozygous (+/-) mutations.

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

- VDR Bsm
- MAO-A R297R
- CBS C699T

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

- COMT V158M
- COMT H62H
- MTR A2756G
- MTRR A66G
- MTRR A664A
- BHMT-02
- BHMT-08
- AHCY-01
- AHCY-19

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.

BHMT mutations

BHMT (betaine homocysteine methyltransferase) acts as a shortcut through the methylation cycle helping convert homocysteine to methionine. The activity of the enzyme can be negatively influenced by stress. The Information on this enzyme related to methylation is mostly based on Dr. Amy Yasko's clinical experience and research.

According to Dr. Yasko, a homozygous mutation of BHMT 01, BHMT 02, BHMT 04, can produce results similar to one with a CBS upregulation even if you don't have a CBS upregulation. In her book, Autism: Pathways to Recovery, She also states that a BHMT 08 mutation may "increase MHPG levels relative to dopamine breakdown (HVA)". This can result in attention type symptoms. It is common to see elevated glycine in someone with a homozygous BHMT 08 mutation.

AHCY Mutations

AHCY (S-adenosylhomocysteine hydrolase) is involved in breaking down the amino acid methionine. It controls the step that converts S-adenosylhomocysteine hydrolase to adenosine and homocysteine. Adenosine plays an important role in energy transfer as ATP and ADP. It helps promote sleep and suppress arousal. Dysfunction of this enzyme can affect levels of homocysteine and ammonia. Some physicians claim AHCY mutations may actually take the strain off the CBS enzyme and may even prevent taurine from becoming very elevated.



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