MOOD PROFILE PANEL

Genetic Analysis Report

Patient Name:	NA	**Date Sample Collected:**	09/20/19
DOB:	NA	**Date Sample Received/Tested:**	09/24/19
Lab ID Number:	1900000000HLA	**Date Reported:**	09/25/19
Ordering Physician:	NA	**Ordering Facility:**	NA

Genes Tested:
MTHFR – C677T/A1298C
COMT – Val158Met
VITAMIN B12 – FUT2
VITAMIN D – GC, NADSYN1/DHCR7, CYP2R1

KEY: **GREEN: NON-RISK ALLELE** **RED: RISK ALLELE**

COMT Mutation Val158Met

COMT
Results: **G/G**

INDICATIONS

Val158Met
G/G homozygous allele carriers typically have higher enzyme activity and lower dopamine levels[1]

BACKGROUND

The COMT (catechol-*O*-methyltransferase) gene codes for an enzyme that is essential for the breakdown of several mood-associated neurotransmitters, most notably dopamine.[1-4] Scientific research has demonstrated that a common mutation in COMT results in the conversion of the amino acid valine to methionine at position 158, and causes a dramatic reduction in the enzyme's ability to break down neurotransmitters. The enzyme is predominantly active in the prefrontal cortex, or PFC; the area of the brain that gives rise to what we perceive as our personality, emotions, behavior inhibition, abstract thinking, and short-term memory.

G/G Val158 allele carriers typically have higher enzyme activity resulting in lower dopamine levels. This may be associated with reduced pre-frontal cognitive function.[4] This allele is also reported to be associated with propensity towards drug abuse and schizophrenia.[4]
A/A Met158 allele carriers have diminished enzyme activity and are more likely to have higher dopamine and norepinephrine levels, associated with higher alcohol intake, OCD, panic disorder, PTSD severity, phobic avoidance, and bipolar affective disorder.[4,5]

References

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Folate (Vitamin B9)
MTHFR Mutations

MTHFR-1: C677T
Results: **T/T**

MTHFR-2: A1298C
Results: **A/A**

INDICATIONS

MTHFR-1: C677T
T/T Homozygous allele carriers are associated with increased homocysteine levels and a higher risk of depression, schizophrenia, and bipolar disorder

MTHFR-2: A1298C
A/A Homozygous allele carriers have full enzymatic activity and typically are not associated with increased risk of depression or high levels of homocysteine

BACKGROUND

The MTHFR (methylenetetrahydrofolate reductase) gene produces an enzyme that helps in processing folate and regulating homocysteine levels in the body. Folate is a critical nutrient involved in methylation, DNA synthesis and amino acid metabolism. Impaired folate metabolism due to MTHFR enzyme inactivity, or decreased folate, results in elevated plasma homocysteine which has been linked to depression.[1-3] The first of two common mutations in the MTHFR gene is the C677T polymorphism.[4] This mutation is characterized by a cytosine (C) to thymine (T) transition at position 677. The second mutation is a substitution of adenine (A) with cytosine (C) at position 1298.[5,6] Elevated homocysteine levels are inversely associated with memory score,[7] and directly related to brain atrophy[8] and depressive symptoms.[1,3] Folate levels are directly related to memory scores,[7] and inversely related to depressive symptoms in women.[2]

C677T
T/T homozygous allele carriers are associated with a higher risk of depression, schizophrenia, and bipolar disorder as compared to the **C/C** genotype.[3,9,10] Depressed, schizophrenic, and bipolar individuals showed a trend towards increased frequency of the T allele, therefore **C/T** heterozygous allele carriers may have an intermediate risk for depression.[9,10]

A1298C
C/C homozygous allele carriers are reported to have an increased risk of depression compared to homozygous non-variant allele carriers[10] **C/C** homozygotes showed an increased risk of schizophrenia compared to homozygous allele carriers **A/A**, while **A/C** heterozygous allele carriers did not show an increased risk of schizophrenia or depression.[10]

References

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Vitamin B12 **FUT2 Mutation**	**BACKGROUND**
FUT2 Results: **A/G**	Genetic variants of the FUT2 gene give rise to a non-functional FUT2 enzyme resulting in an inability to synthesize ABH blood group antigens on mucosal surfaces which is referred to as a 'non-secretor status'.[1] The non-secretor phenotype has been associated with higher vitamin B12 levels than the secretor phenotype.[2,7] Low B12 vitamin status has long been linked to depressive behavior.[3,4] Vitamin B12 supports the synthesis of a molecule known as S-adenosylmethionine (SAM) which is critical in regulating levels of neurotransmitters in the brain.[5] Scientific research suggests that B12 deficiency may contribute to a reduction in SAM leading to chemical imbalances in the brain resulting in depression. More recently, a large population based study reported that there was an approximately three-fold increase in risk for melancholic depressive symptoms in individuals with low B12 levels.[6]
INDICATIONS	
A/A and **A/G** allele carriers are associated with higher vitamin B12 concentrations	**A/A** and **A/G** individuals have been shown to have decreased function of the enzyme generating a non-secretor status, increased vitamin B12 levels, and therefore no significant association with increased risk for mood disorders.[6] **G/G** individuals generally have lower vitamin B12 levels, the latter being associated with depressive behavior, and specifically melancholic depressive symptoms.[6]

References

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Vitamin D CYP2R1 Mutation	BACKGROUND
CYP2R1 Results: **A/A** **INDICATIONS** **A/A** Homozygous carriers of no risk alleles had significantly higher vitamin D levels	A locus containing a single nucleotide polymorphism (SNP) associated with vitamin D levels, the CYP2R1 gene encodes the hepatic enzyme 25-hydroxylase suggested to be responsible for the hydroxylation step of vitamin D metabolism in the liver.[1] The polymorphism is located in a coding region of this gene and may change the activity of the enzyme leading to a lowered 25(OH)D level.[2,3] Low vitamin D levels have been shown to be associated with impairments in cognitive function, and increased risk of developing depression in patients,[4,5] suggesting these variants can be used to indicate potential risk of mood disorders associated with low vitamin D levels. **A/A** individuals have been shown to have higher vitamin D serum levels and therefore may not be at increased risk for the development of depression. **A/G** and **G/G** individuals are more likely to have vitamin D insufficiency and be prone to developing depression.

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Vitamin D NADSYN1/DHCR7 Mutation	BACKGROUND
NADSYN1/DHCR7 Results: **T/G** **INDICATIONS** **T/G** Heterozygotes may have higher levels of serum vitamin D	*NADSYN1/DHCR7* is a novel locus for association with vitamin D status, but with direct biological relevance. A G->T SNP is found in an intron of NADSYN1 (nicotinamide adenine dinucleotide synthase 1), a gene that catalyzes the final step of NAD biosynthesis.[1] This SNP is in high linkage disequilibrium with SNPs in DHCR7 (7-dehydrocholesterol reductase), a gene that encodes the enzyme 7-dehydrocholesterol reductase, which converts the vitamin D precursor (7-DHC) to cholesterol.[2] By converting the 7-DHC into cholesterol, the needed substrate used by the body to generate vitamin D is removed, leaving the individual at a higher risk of vitamin D deficiency.[3] Low vitamin D levels have been shown to be associated with impairments in cognitive function, and increased risk of developing depression in patients,[4,5] suggesting these markers can be used to indicate potential risk of mood disorders associated with low vitamin D levels. **T/T** and **T/G** allele carriers are reported to have higher levels of circulating 25(OH)D and lower frequency of vitamin D insufficiency, dyslipidemia, and less risk of developing depression than G/G allele carriers.[3-5] **G/G** homozygous individuals are associated with a greater risk of vitamin D insufficiency and therefore may be more prone to developing mood disorders.[3-5]

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VITAMIN D GC Mutations	BACKGROUND
Haplotype Results: **G/C**; **T/A**	The GC gene encodes the group-specific component protein, also referred to as the vitamin D binding protein, which functions to tightly bind and carry vitamin D metabolites to their target organs. A two-SNP combination in this gene is directly associated with variability in vitamin D [25(OH)D] concentrations.[1-4] These well-studied GC SNP variants result in allelic combinations (haplotypes) that give rise to three common GC isoforms, GC1F, GC1S, and GC2.[1] These variants in particular, change the amino acid sequence and alter protein function. Several studies have shown that vitamin D serum levels differ significantly depending on the GC genotype.[3,5] Without sufficient vitamin D, bones can become brittle or misshapen, leading to osteoporosis and/or fracture.[6] Maintaining adequate levels of vitamin D may be beneficial to patients not only for optimal bone health, but also for reducing cardiovascular and autoimmune disease, cancer risk, and increasing life expectancy.[6,7]
INDICATIONS Individuals with the **G/C** haplotype (GC1s isoform), have an intermediate risk for vitamin D deficiency, while the **T/A** haplotype (GC2 isoform), usually is associated with an increased risk of vitamin D deficiency. Having one allele of each may result in an intermediate to elevated risk of vitamin D deficiency.	**Isoforms:** **GC1f** is considered the non-risk isoform and has the highest affinity for 25(OH)D. Individuals with this genotype are not associated with increased risk for vitamin D deficiency.[1] **GC1s** has intermediate affinity for 25(OH)D, individuals with this genotype have an intermediate risk profile for vitamin D deficiency.[1] **GC2** has the lowest affinity for 25(OH)D, and it is suggested that individuals with this genotype have lower vitamin D concentrations due to reduced binding capacity of the transport protein, and thus may be at risk for vitamin D deficiency.[1] Limitations Less common variants of GC are not reported by this test. While considered rare, the presence of these variants may result in a false positive or false negative report. If results obtained do not match the clinical findings, additional testing should be considered. All results should be interpreted in the context of clinical findings, relevant history, and other laboratory findings

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This test detects only specific targeted genetic variations and there is a possibility that other genetic variants not detected by this test may be present. The DNA variants tested for in this report have been scientifically determined to be possible risk factors for the reported condition. The content of this report is provided for informational purposes only, not as a diagnostic tool. The report does not supersede the judgment of a qualified medical provider. This test is not a substitute for a comprehensive consideration of all factors that influence the maintenance of a healthy body. Genetic risk factors are not guarantees that you will develop a condition, and in many cases, the presence of a particular DNA variant may only play a minor role in your risk for disease, compared with environmental and lifestyle factors. This test is not FDA approved. The test's performance characteristics have been established and maintained by Kashi Clinical Laboratories under CLIA and CAP compliance

Reported and Reviewed By:

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