COMT

Genetic Analysis Report

PATIENT	ORDERING PROVIDER	LABORATORY INFORMATION	
PFirst PLast	Example Organization	Lab ID:	N8C9841
DOB: 01/01/72		Collection Date:	01/11/10
		Test Date:	01/21/10
		Report Date:	01/22/10

COMT GG

The patient's genotype for COMT suggests rapid breakdown of catecholamines, most notably dopamine. A patient with this genotype may require higher doses of pain medication. A diet high in tyrosine may support continuous neurotransmitter production. Some research has found that the polyphenols EGCG and quercetin may inhibit the COMT enzyme.

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ASSAY	RESULT	PHENOTYPE	ENZYME ACTIVITY
COMT	G/G	Normal	High

CLINICAL CONSEQUENCES

Homozygous Val/Val allele carriers exhibit higher COMT enzyme activity and thus have an increased capacity to degrade catecholamines; this can contribute to lower dopamine levels and a higher pain tolerance. Despite being more resilient to pain, Val/Val genotypes often require higher doses of morphine to obtain the same pain relief as other genotypes. Val/Val allele carriers may have an enhanced response to COMT inhibitors used in Parkinson's disease treatment and may have lower estradiol levels than those expressing other alleles.

COMT BACKGROUND INFORMATION

The COMT (catechol-O-methyltransferase) gene codes for the essential COMT enzyme that is involved in the inactivation of catecholamines such as dopamine, epinephrine, norepinephrine and catecholestrogens.[1-3] Scientific research has demonstrated that a common mutation in the COMT locus results in the replacement of the amino acid valine with methionine at position 158 in the enzyme. This causes a dramatic reduction in the enzyme's ability to metabolize these neurotransmitters and catecholestrogens.[1,4] The enzyme is notably active in the prefrontal cortex (PFC), the area of the brain that gives rise to what we perceive as personality, emotions, behavior inhibition, abstract thinking, and short-term memory.[5] Val/Val allele carriers have higher enzyme activity resulting in greater stress resiliency and lower dopamine levels, while Met/Met allele carriers have lower enzyme activity resulting in reduced stress resiliency and higher dopamine levels. Heterozygous Val/Met allele carriers exhibit an intermediate enzyme activity. Polymorphisms in the COMT gene have been implicated in association with various mental health disorders through the resulting changes in dopamine levels.[1,2,5,6] Depending on the variant, associated disorders include drug abuse,[7] alcohol abuse,[8] severity of schizophrenic symptoms,[9,10] obsessive compulsive disorder in men,[11] panic disorder,[12] post-traumatic stress disorder,[13] and bipolar affective disorder.[14,15] Having a particular polymorphism does not mean that someone will develop one or more of the associated disorders.

Summary of Likely Patterns Associated with COMT Alleles

GENE ALLELE	ENZYME ACTIVITY	DOPAMINE LEVELS	PAIN RESPONSE	PAIN MED NEED	STRESS RESILIENCY	ESTRADIOL LEVELS
Val/Val	HIGH	LOWER	MORE TOLERANCE	POSSIBLE HIGHER DOSE	HIGHER	LIKELY LOWER
Val/Met	BALANCED	AVERAGE	AVERAGE	AVERAGE	AVERAGE	AVERAGE
Met/Met	LOW	HIGHER	MORE ACUTE	PROBABLY LOWER DOSE	REDUCED	LIKELY HIGHER

PAIN MANAGEMENT AND NEUROLOGICAL INFORMATION

COMT polymorphisms have been linked to pain sensitivity.[16,17] It has been suggested that a reduction in dopamine inactivation, such as is seen with the Met/Met genotype, results in higher levels of dopamine, leading to chronic stimulation of the dopamine receptors. This overstimulation may result in less endogenous opioids being produced that help to provide pain relief and euphoria.[17] Therefore, Met/Met allele carriers can perceive a higher level of pain, while Val/Val carriers have the greatest resistance to pain.[16,17] Interestingly, studies have shown that Met/Met allele carriers require less morphine to achieve pain relief, possibly due to the increase in μ-opioid receptors seen with this genotype, while Val/Val allele carriers require the most medication for pain management.[18] COMT also has been shown to have an effect on L-DOPA therapy in Parkinson's disease treatment.[19] Commonly COMT inhibitors, such as entacapone, are utilized in Parkinson's treatment to augment and prolong L-DOPA treatment.[20] COMT polymorphisms affect the bioavailability of these medications, yielding a heightened effect of entacapone in the Val/Val allele carriers as compared to Met/Met allele carriers.

ESTRADIOL INFORMATION

COMT has also been demonstrated to play a role in estrogen metabolism through inactivation of the catecholestrogens.[21] Catecholestrogens are formed during the metabolism of estrogens such as estradiol. Catecholestrogen inactivation decreases the cancer-causing potential of these metabolites, while simultaneously increasing the amount of 2-methoxyestradiol, a metabolite that has been shown to inhibit the growth of breast cancer cells.[4,22,23] Additionally, COMT polymorphisms have been shown to exert an effect on estradiol levels.[24] As Met/Met allele carriers exhibit a 2-3 fold decrease in their ability to degrade catecholestrogens, this results in higher estradiol levels than Val/Val allele carriers.[4,25] Estradiol clearance is also diminished in both the Met/Met and Met/Val genotypes as opposed to Val/Val genotypes, however there is no significant difference in estrone levels.[24]

TREATMENT CONSIDERATIONS

Homozygous Valine (Val/Val) allele carriers have lower dopamine levels. Increasing certain amino acids without proper balance of all neurotransmitters may result in increased cognitive symptoms.[32]

- L-Tyrosine is an amino acid and a precursor to dopamine. [33] Dopamine precursors may be supportive of dopamine production; however, L-tyrosine's use in the treatment of individuals with the Val/Val genotype is theoretical as there have been no studies performed validating its effectiveness.
- COMT polymorphisms, specifically Val/Val homozygotes, may influence the plasma levels of homocysteine. [44] Individuals with high levels of homocysteine may benefit from supplementation with melatonin, which may lower homocysteine. [45]
- Active B Complex vitamins are associated with the proper methylation of enzymes throughout the body and may lower homocysteine, while high levels of homocysteine are associated with cognitive impairment.[28-31]
- Green tea may suppress COMT function, increase dopamine release, and suppress the production of reactive oxygen species, thereby inhibiting inflammatory responses. [46-49] Additionally, intake of caffeine may support dopamine neurotransmission in conditions with dopamine deficiency.[50]
- A small study in elderly adults found that increasing unsaturated fatty acids along with caloric restriction modulates cognition in homozygous (Val/Val) allele carriers.[51]
- A small study in elderly adults found that physical activity improves cognition in homozygous (Val/Val) allele carriers.[52]

NOTICE: This information does not take into consideration patient health history, interaction with other medications or supplements, and/or allergies. It is the responsibility of the physician to determine appropriate dosing choices based on all clinical data.

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.

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