KASHI CLINICAL LABORATORIES

COMT Genotyping
Healthcare Professional Information

COMT: Understand your Patient's Risk & Health Implications

Estrogen metabolism is crucial to proper bio-identical hormone management. Whether considering estrogen dominance or breast cancer risk, COMT genotyping can help to inform your patient's treatment options.

Bio-identical hormone therapy is a very supportive tool to help patients with various health complaints. From menopausal symptoms, to weight gain, to fatigue - many patients find the use of hormone therapy to be nothing short of a miracle to improving the quality of their everyday life. However, the use of these hormones can increase cancer risk in some patients. So how can you tailor this to be the safest treatment for your patients as possible? Personal and family history for cancer risk and well as hormone level monitoring is a very good first step. Introduction of the COMT genetic test helps to further inform your patient's risk.

The COMT (catechol-O-methyltransferase) gene codes for the essential COMT enzyme that is involved in the inactivation of the catecholestrogens.[1] Scientific research has demonstrated that a common mutation in the COMT gene resulting in the conversion of the amino acid valine to methionine at position 158 (Val158Met) causes a dramatic reduction in the enzyme's ability to metabolize these catecholestrogens.[2] Homozygous Valine (Val/Val) allele carriers have higher enzyme activity, while homozygous Methionine (Met/Met) allele carriers have lower enzyme activity, and heterozygous Val/Met allele carriers exhibit an intermediate enzyme activity.

This change in enzyme activity has been shown to play a role in estrogen metabolism through a change in the inactivation of the catecholestrogens.[3] The COMT enzyme performs this inactivation step by converting hydroxylated estrogens into methoxylated estrogens by the addition of a methyl group. This process lowers 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.[2,4,5] Additionally, COMT polymorphisms have been shown to influence estradiol levels, the most potent of the various estrogen forms.[6] Met/Met and Met/Val allele carriers exhibit a 2-3 fold decrease in their ability to degrade catecholestrogens, resulting in higher estradiol levels than the Val/Val allele carriers.[2,7]

TESTING YOUR PATIENT'S DNA CAN HELP TO TRULY INDIVIDUALIZE THEIR BIO-IDENTICAL HORMONE THERAPY. UNDERSTANDING YOUR PATIENT'S GENOTYPE CAN HELP TO INFORM THEIR RISK OF ACQUIRING BREAST CANCER AS WELL AS INFLUENCES ON THEIR INDIVIDUAL ESTRADIOL LEVELS.

References:

1. Mannisto P and S Kaakkola. Catechol-O-methyltransferase (COMT): Biochemistry, Molecular Biology, Pharmacology, and Clinical Efficacy of the New Selective COMT Inhibitors. Pharm Rev. 1999; 51(4):594-622.
2. Dawling S et al. Catechol-O-Methyltransferase (COMT)-mediated Metabolism of Catechol Estrogens: Comparison of Wild-Type and Variant COMT Isoforms. Cancer Res. 2001; 61:6716-6722.
3. Ball P and R Knuppen. Catecholoestrogens (2-and 4-hydroxyoestrogens): chemistry, biogenesis, metabolism, occurrence and physiological significance. Acta Endocrinol. Suppl. (Copenh). 1980; 232:1-127.
4. Lakhani NJ et al. 2-Methoxyestradiol, a Promising Anticancer Agent. Pharmacotherapy. 2003; 23:165-172.
5. Lavigne JA et al. The Effects of Catechol-O-Methyltransferase Inhibition on Estrogen Metabolite and Oxidative DNBA Damage Levels in Estradiol-treated MCF-7 Cells. Cancer Research. 2001; 61:7488-7494.
6. Worda C et al. Influence of the catechol-O-methyltransferase (COMT) codon 158 polymorphism on estrogen levels in women. Human Reproduction. 2003; 18(2):262-266.
7. Eriksson AL et al. The COMT val158met polymorphism Is Associated with Early Pubertal Development, Height and Cortical Bone Mass in Girls. Pediatr Res. 2005; 58(1):71-77.