Kashi Clinical Laboratories, Inc.
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KASHI HEALTH

Delivering More Than a Test Result

ASHI No. 10-4-OR-03-1
CLIA No. 38D1058476

COMT GENOTYPING REPORT

Patient Name:	Johnny Health	Date Sample Collected:	00/00/14
DOB:	00/00/14	Date Sample Received/Tested:	00/00/14
Lab ID Number:	000000000	Date Reported:	00/00/14
Ordering Physician:	Dr. KCL	Ordering Facility:	Acme Center

PATIENT'S TEST RESULTS AND INDICATIONS

TEST	GENOTYPE	RESULT
Val158Met Mutation	G/G	Val/Val

This patient carries a Val158Met gene mutation resulting in Homozygous Val/Val alleles.

- Typically exhibit a higher enzyme activity, with greater stress resiliency.
- Lower dopamine levels.
- May have a greater resistance to pain, yet may have a greater requirement for morphine in pain relief.
- May have an enhanced response to a COMT inhibitors used in Parkinson's disease treatment as compared to Met/Met allele carriers.
- Indicates a greater capacity to degrade catecholestrogens and may have lower estradiol levels as compared to Met/Met and Val/Met genotypes.

PATIENT'S APPROXIMATE COMT ENZYME ACTIVITY[2]

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 and norepinephrine and catecholestrogens.[1-3] Scientific research has demonstrated that a common mutation in the COMT locus 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 metabolize these neurotransmitters and catecholestrogens.[1,4] The enzyme is notably 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.[5] Val allele carriers have higher enzyme activity resulting in greater stress resiliency and lower dopamine levels, while Met allele carriers have lower enzyme activity resulting in reduced stress resiliency and higher dopamine levels, and heterozygous Val/Met allele carriers exhibit an intermediate enzyme activity.

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MENTAL HEALTH

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] Disorders that may be associated with this gene variant in some populations 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]

PAIN MANAGEMENT INFORMATION AND NEUROLOGICAL INFORMATION

COMT polymorphisms have also 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 perceive a higher level of pain, while Val/Val carriers have the greatest resistance to pain.[16,17] Interestingly though, 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 an enhanced 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] This inactivation step 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.[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]

This test was developed and its performance characteristics determined by Kashi Clinical Laboratories. It has not been cleared or approved by the FDA. The laboratory is regulated under CLIA as qualified to perform high-complexity testing. This test is used for clinical purposes. It should not be regarded as investigational or for research.

Reported and Reviewed By:

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CEO and Laboratory Director

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COMT TREATMENT OPTIONS

NOTICE: These recommendations do 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.

	Supplement	Starting Dosage Range	Notes
✓	S-adenosyl methionine (SAMe)	400-1,600 mg/day	SAMe is an important methyl group donor involved in many of the biochemical and enzyme structures in the body. Specifically, it is involved in the synthesis of the COMT enzyme and involved in folate metabolism. Additionally, SAMe may be useful in the treatment of depression. [26-29]
✓	Magnesium	200-600 mg/day, or to bowel tolerance.	Magnesium is required for the proper synthesis of the COMT enzyme in addition to proper function many other enzyme complexes throughout the body. Deficiency is associated with depression and poor cognition. [30-33]
✓	Active B Complex	Daily RDA or 50 mg BID	Active B Complex vitamins are associated with proper methylation of enzymes throughout the body and may lower homocysteine, which is associated with cognitive impairment.[34-37]

OPTIONAL DEPENDING ON HEALTH CONDITIONS AND PROVIDER DISCRETION

Homozygous Valine (Val/Val) allele carriers have lower dopamine levels. Increasing certain amino acids without proper balance of all neurotransmitters will further the depletion of dopamine and result in increased cognitive symptoms.[38-39]

- **L-Tryptophan** is an essential amino acid and precursor to melatonin and serotonin and building block for proteins. This may be effective for patients with a deficiency in serotonin levels and depression.[40-41]
- **L-5-Hydroxytryptophan (5-HTP)** is a metabolite of L-tryptophan and the precursor to serotonin. 5-HTP bypasses the rate-limiting enzyme in serotonin synthesis. Supplementation of 5-HTP may be useful as adjunctive treatment for depression.[42-43]
- **L-Theanine** is a constituent and amino acid found in green tea that has demonstrated improvement in cognitive function in neurological conditions.[44-47]
- **N-Acetyl-cysteine** is a precursor to glutathione and thiolic antioxidant, which may be beneficial for the nervous system, inflammatory conditions, and in dopamine and estrogen deficient conditions.[48-50]

RECOMMENDED LIFESTYLE INTERVENTIONS

• **Avoid L-Tyrosine and L-Dopa supplements, and excessive vitamin C.** L-tyrosine is a large neutral amino acid and precursor to catecholamines, and is synthesized from phenylalanine. L-Dopa is also a precursor to catecholamine synthesis, which requires ascorbate to synthesize norepinephrine from dopamine.[51-52]

• **Foods that contain tyramine, such as cheese and wine, may be converted into dopamine endogenously and may trigger dopamine release and catecholamines.** Tyramine is a trace amine synthesized from enzymatic conversion of tyrosine.[53-55]

• **COMT polymorphisms, specifically Val/Val homozygotes, may influence the plasma levels of homocysteine levels.** Individuals with high levels of homocystein may benefit from supplementation of melatonin, which may lower homocysteine.[56-57]

• **Green tea may suppress COMT function, increase dopamine release, and suppress the production of reactive oxygen species, thereby inhibiting inflammatory responses.** Additionally, intake of caffeine may modulate dopamine neurotransmission in conditions with dopamine deficiency.[58-62]

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RECOMMENDED LIFESTYLE INTERVENTIONS (Continued)

- **Increasing unsaturated fatty acids and caloric restriction modulates cognition in homozygous (Val/Val) allele carriers.** [63]
- **Physical activity improves cognition in homozygous (Val/Val) allele carriers.**[64]

Additional Vitamins

- Selenium supplementation may improve health outcomes in deficiency states. [65-67]

Background References:

1. Lachman H et al. Human catechol-O-methyltransferase pharmacogenetics: description of a functional polymorphism and its potential application to neuropsychiatric disorders. Pharmacogenetics 1996; 6:243-250.
2. Weinshilboum R et al. Methylation Pharmacogenetics: Catechol-O methyltransferase, Thiopurine Methyltransferase, and Histamine N-Methyltransferase. Annu. Rev. Pharmacol. Toxicol. 1999; 39:19-52.
3. 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.
4. 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.
5. Mier D et al. Neural substrates of pleiotropic action of genetic variation in COMT: a meta-analysis. Molecular Psychiatry. 2010; 15:918-927.
6. Goldman D et al. The Genetics of Addictions: Uncovering the Genes. Nat Rev Genet. 2005; 6(7):521-532.
7. Yuferov V et al. Search for Genetic Markers and Functional Variants Involved in the Development of Opiate and Cocaine Addiction, and Treatment. Ann N Y Acad Sci. 2010; 1187:184-207.
8. Schellekens AF et al. COMT Val158Met modulates the effect of childhood adverse experiences on the risk of alcohol dependence. Addict Biol. 2013; 18(2):344-356.
9. Bhakta SG et al. The COMT Met158 allele and violence in schizophrenia: a meta-analysis. Schizophr Res. 2012; 140(1-3):192-197.
10. Godar SC and M Bortolato. Gene-sex interactions in schizophrenia: focus on dopamine neurotransmission. Front Behav Neurosci. 2014; 8:71.
11. Pooley EC et al. The met158 allele of catechol-o-methyltransferase (COMT) is associated with obsessive-compulsive disorder in men: case-control study and meta-analysis. Mol Psych. 2007; 12:556-551.
12. Konishi Y et al. Genexgenexgender interaction of BDNF and COMT genotypes associated with panic disorder. Prog Neuropsychopharmacol Biol Psychiatry. 2014; 51:119-125.
13. Kolassa IT et al. The risk of posttraumatic stress disorder after trauma depends on traumatic load and the catechol-o-methyltransferase Val(158)Met polymorphism. Biol Psychiatry. 2010; 67(4):304-308.
14. Lee SY et al. COMT and BDNF interacted in bipolar II disorder not comorbid with anxiety disorder. Behav Brain Res. 2013; 237:243-248.
15. Zhang Z. The Val/Met functional polymorphism in COMT confers susceptibility to bipolar disorder: evidence from an association study and a meta-analysis. J Neural Transm. 2009; 116(10):1193-200.
16. Janicki PK. Pharmacogenetics of Pain Management. Comprehensive Treatment of Chronic Pain by Medical, Interventional, and Integrative Approaches. Edited by TR Deers. American Academy of Pain Medicine. 2013.
17. Zubieta JK et al. COMT val158met Genotype Affects mu-opioid Neurotransmitter Responses to a Pain Stressor. Science. 2003; 299(5610):1240-1243.
18. Klepstad P et al. Genetic variability and clinical efficacy of morphine. Acta Anasthesiol Scand. 2005; 49:902-908.
19. Mannisto PT 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.
20. Corvol JC et al. The OCMT Val158Met polymorphism affects the response to entacapone in Prakinson's disease: a randomized crossover clinical trial. Ann Neurol. 2011; 69(1):111-118.
21. 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.
22. Lakhani NJ et al. 2-Methoxyestradiol, a Promising Anticancer Agent. Pharmacotherapy. 2003; 23:165-172.
23. 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.
24. 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.
25. 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.

Treatment References:

26. Li Y, Yang X, Chang M, Yager JD, Van Breemen RB, Bolton JL. Functional and structural comparisons of cysteine residues in the Val108 wild type and Met108 variant of human soluble catechol O-methyltransferase. *Chem Biol Interact*. 2005;152(2-3):151-163. doi:10.1016/j.cbi.2005.03.001.
27. Bailey LB, Gregory JF. Recent Advances in Nutritional Science Folate Metabolism and. *J Nutr*. 1999;129:779-782.
28. Sarris J, I. Papakostas G, Vitolo O, Fava M, Mischoulon D. S-adenosyl methionine (SAMe) versus escitalopram and placebo in major depression RCT: Efficacy and effects of histamine and carnitine as moderators of response. *J Affect Disord*. 2014;164:76-81. doi:10.1016/j.jad.2014.03.041.
29. Fava M, Giannelli A, Rapisarda V, Patralia A, Guaraldi GP. Rapidity of onset of the antidepressant effect of parenteral S-adenosyl-l-methionine. *Psychiatry Res*. 1995;56(3):295-297. doi:10.1016/0165-1781(95)02656-H.
30. Li Y, Yang X, Chang M, Yager JD, Van Breemen RB, Bolton JL. Functional and structural comparisons of cysteine residues in the Val108 wild type and Met108 variant of human soluble catechol O-methyltransferase. *Chem Biol Interact*. 2005;152(2-3):151-163. doi:10.1016/j.cbi.2005.03.001.
31. Sowa-Kucma M, Szewczyk B, Sadlik K, et al. Zinc, magnesium and NMDA receptor alterations in the hippocampus of suicide victims. *J Affect Disord*. 2013;151(3):924-931. doi:10.1016/j.jad.2013.08.009.
32. Basheer MP, Pradeep Kumar KM, Sreekumaran E, Ramakrishna T. A study of serum magnesium, calcium and phosphorus level, and cognition in the elderly population of South India. *Alexandria J Med*. 2015. doi:10.1016/j.ajme.2015.11.001.
33. Yary T, Lehto SM, Tolmunen T, et al. Dietary magnesium intake and the incidence of depression: A 20 year follow-up study. *J Affect Disord*. 2016;193:94-98. doi:10.1016/j.jad.2015.12.056.
34. Haan MN, Miller JW, Aiello AE, et al. Homocysteine, B vitamins, and the incidence of dementia and cognitive impairment: Results from the Sacramento Area Latino Study on Aging. *Am J Clin Nutr*. 2007;85(2):511-517. doi:85/2/511 [pii].
35. Smith AD, Smith SM, de Jager CA, et al. Homocysteine-lowering by b vitamins slows the rate of accelerated brain atrophy in mild cognitive impairment: A randomized controlled trial. *PLoS One*. 2010;5(9):1-10. doi:10.1371/journal.pone.0012244.
36. Mitchell ES, Conus N, Kaput J. Neuroscience and Biobehavioral Reviews B vitamin polymorphisms and behavior : Evidence of associations with neurodevelopment , depression , schizophrenia , bipolar disorder and cognitive decline. *Neurosci Biobehav Rev*. 2014;47:307-320. doi:10.1016/j.neubiorev.2014.08.006.
37. Kennedy DO, Veasey R, Watson A, et al. Effects of high-dose B vitamin complex with vitamin C and minerals on subjective mood and performance in healthy males. *Psychopharmacology (Berl)*. 2010;211(1):55-68. doi:10.1007/s00213-010-1870-3.
38. Masurier M Le, Oldenzeil W, Lehman C, Cowen P, Sharp T. Effect of Acute Tyrosine Depletion in Using a Branched Chain Amino-Acid Mixture on Dopamine Neurotransmission in the Rat Brain. 2006:310-317. doi:10.1038/sj.npp.1300835.
39. De Simone R, Vissicchio F, Mingarelli C, et al. Branched-chain amino acids influence the immune properties of microglial cells and their responsiveness to pro-inflammatory signals. *Biochim Biophys Acta - Mol Basis Dis*. 2013;1832(5):650-659. doi:10.1016/j.bbadis.2013.02.001.
40. Myint AM, Kim YK, Verkerk R, Scharpé S, Steinbusch H, Leonard B. Kynurenine pathway in major depression: Evidence of impaired neuroprotection. *J Affect Disord*. 2007;98(1-2):143-151. doi:10.1016/j.jad.2006.07.013.
41. Reus GZ, Jansen K, Titus S, Carvalho AF, Gabbay V, Quevedo J. Kynurenine pathway dysfunction in the pathophysiology and treatment of depression: Evidences from animal and human studies. *J Psychiatr Res*. 2015;68:316-328. doi:10.1016/j.jpsychires.2015.05.007.
42. Jangid P, Malik P, Singh P, Sharma M, Gulia A kumar D. Comparative study of efficacy of l-5-hydroxytryptophan and fluoxetine in patients presenting with first depressive episode. *Asian J Psychiatr*. 2013;6(1):29-34. doi:10.1016/j.ajp.2012.05.011.
43. Lowe SL, Poo Yeo K, Teng L, et al. L-5-Hydroxytryptophan augments the neuroendocrine response to a SSRI. *Psychoneuroendocrinology*. 2006;31(4):473-484. doi:10.1016/j.psyneuen.2005.11.005.
44. Lardner AL. Neurobioligical effects of the green tea constituent theanine and its potential role in the treatment of psychiatric and neurodegenerative disorders. *Nutritional Neuroscience*. 2014;17(4): 145-155.
45. Mu W, Zhang T, Jiang B. An overview of biological production of L-theanine. *Biotechnol Adv*. 2015;33(3-4):335-342. doi:10.1016/j.biotechadv.2015.04.004.
46. Kakuda T. Neuroprotective effects of theanine and its preventive effects on cognitive dysfunction. *Pharmacol Res*. 2011;64(2):162-168. doi:10.1016/j.phrs.2011.03.010.
47. Tian X, Sun L, Gou L, et al. Protective effect of l-theanine on chronic restraint stress-induced cognitive impairments in mice. *Brain Res*. 2013;1503:24-32. doi:10.1016/j.brainres.2013.01.048.
48. Martínez-Banaclocha MA. N-acetyl-cysteine in the treatment of Parkinson's disease. What are we waiting for? *Med Hypotheses*. 2012;79(1):8-12. doi:10.1016/j.mehy.2012.03.021.
49. Dean OM, Van Den Buuse M, Berk M, Copolov DL, Mavros C, Bush AI. N-acetyl cysteine restores brain glutathione loss in combined 2-cyclohexene-1-one and d-amphetamine-treated rats: Relevance to schizophrenia and bipolar disorder. *Neurosci Lett*. 2011;499(3):149-153. doi:10.1016/j.neulet.2011.05.027.
50. Botsakis K, Theodoritsi S, Grintzalis K, et al. 17β-Estradiol/N-acetylcysteine interaction enhances the neuroprotective effect on dopaminergic neurons in the weaver model of dopamine deficiency. *Neuroscience*. 2016;320:221-229. doi:10.1016/j.neuroscience.2016.01.068
51. Masoud ST, Vecchio LM, Bergeron Y, et al. Increased expression of the dopamine transporter leads to loss of dopamine neurons, oxidative stress and l-DOPA reversible motor deficits. *Neurobiol Dis*. 2015;74:66-75. doi:10.1016/j.nbd.2014.10.016.
52. Lipski J, Nistico R, Berretta N, Guatteo E, Bernardi G, Mercuri NB. L-DOPA: A scapegoat for accelerated neurodegeneration in Parkinson's disease? *Prog Neurobiol*. 2011;94(4):389-407. doi:10.1016/j.pneurobio.2011.06.005.
53. Hiroi T, Imaoka S, Funae Y. Dopamine formation from tyramine by CYP2D6. *Biochem Biophys Res Commun*. 1998;249(3):838-843. doi:10.1006/bbrc.1998.9232.
54. Zhu ZT, Munhall AC, Johnson SW. Tyramine excites rat subthalamic neurons in vitro by a dopamine-dependent mechanism. *Neuropharmacology*. 2007;52(4):1169-1178. doi:10.1016/j.neuropharm.2006.12.005.
55. Burchett SA, Hicks TP. The mysterious trace amines : Protean neuromodulators of synaptic transmission in mammalian brain §. 2006;79:223-246. doi:10.1016/j.pneurobio.2006.07.003.
56. Tunbridge, Elizabeth M., et al. "Polymorphisms in the catechol-O-methyltransferase (COMT) gene influence plasma total homocysteine levels." *American Journal of Medical Genetics Part B: Neuropsychiatric Genetics* 147.6 (2008): 996-999.

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Treatment References:

57. Paul R, Borah A. The potential physiological crosstalk and interrelationship between two sovereign endogenous amines, melatonin and homocysteine. *Life Sci*. 2015;139:97-107. doi:10.1016/j.lfs.2015.07.031.
58. Hursel, R., Pilou, LHR, et al. The Role of Catechol-o-Methyl Transferase Val(108/158) MET Polymophism (rs4680) in the effect of Green Tea on Resting Energy Expenditure and Fat Oxidation: A Pilo Study. 2014.
59. Lorenz M, Paul F, Moobed M, et al. The activity of catechol-O-methyltransferase (COMT) is not impaired by high doses of epigallocatechin-3-gallate (EGCG) in vivo. Eur J Pharmacol. 2014;740:645-651. doi:10.1016/j.ejphar.2014.06.014.
60. Kang KS, Yamabe N, Wen Y, Fukui M, Zhu BT. Beneficial effects of natural phenolics on levodopa methylation and oxidative neurodegeneration. Brain Res. 2013;1497:1-14. doi:10.1016/j.brainres.2012.11.043.
61. Kang KS, Wen Y, Yamabe N, Fukui M, Bishop SC, Zhu BT. Dual beneficial effects of (-)-epigallocatechin-3-gallate on levodopa methylation and hippocampal neurodegeneration: In vitro and in vivo studies. PLoS One. 2010;5(8). doi:10.1371/journal.pone.0011951.
62. Xie X, Ramkumar V, Toth LA. Adenosine and dopamine receptor interactions in striatum and caffeine-induced behavioral activation. Comp Med. 2007;57(6):538-545.
63. Witte AV, Jansen S, Schirmacher A, Young P, Flöel A. COMT Val158Met polymorphism modulates cognitive effects of dietary intervention. Front Aging Neurosci. 2010. doi:10.3389/fnagi.2010.00146.
64. Voelcker-Rehage C, Jeltsch A, Godde B, Becker S, Staudinger UM. COMT gene polymorphisms, cognitive performance, and physical fitness in older adults. Psychol Sport Exerc. 2015;20:20-28. doi:10.1016/j.psychsport.2015.04.001.
65. Hawkes WC, Hornbostel L. Effects of dietary selenium on mood in healthy men living in a metabolic research unit. Biol Psychiatry. 1996;39(2):121-128. doi:10.1016/0006-3223(95)000852.
66. Rayman M, Thompson A, Warren-Perry M, et al. Impact of selenium on mood and quality of life: A randomized, controlled trial. Biol Psychiatry. 2006;59(2):147-154. doi:10.1016/j.biopsych.2005.06.019.
67. Santhosh Kumar B, Priyadarsini KI. Selenium nutrition: How important is it? Biomed Prev Nutr. 2014;4(2):333-341. doi:10.1016/j.bionut.2014.01.006.