



Gene Comprehensive Nutrigenomic Report

Accession Number: #####

Specimen Collected: ##/##/####

Specimen Received: ##/##/####

Report Generated: November 17, 2022

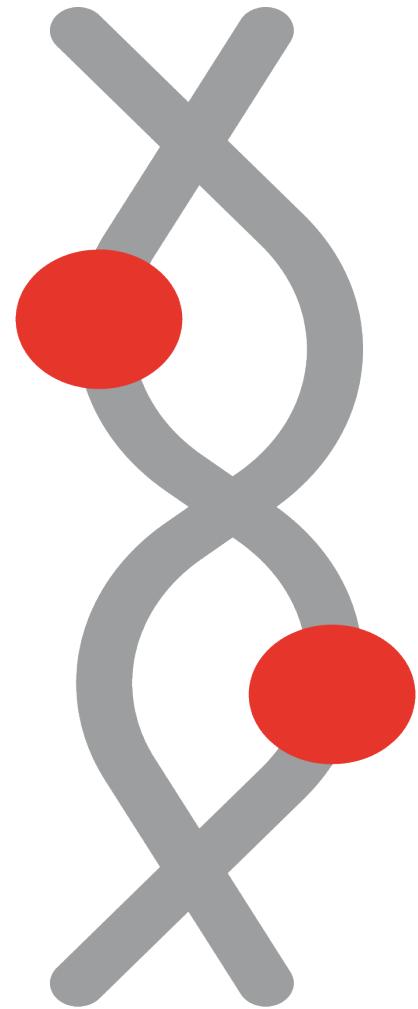
Specimen Type: Buccal Swab

Provider: #####

Patient Name: #####

Patient DOB: ##/##/####

Patient Gender: Male



Do not make any decisions about your health solely based on the information contained in this report.
Always consult with a licensed and experienced health practitioner when you receive this report.

- 36 - Male

(-/-) No clinical abnormality

(+/-) Heterozygous result

(++) Homozygous result

rsID	Gene	Genetic Result	Therapeutics Associated With Positive Result	Highly Recommended Therapeutics	Provider Discretion: As Needed Formula Recommendations	Lifestyle Recommendations	Laboratory Recommendations
Essential Vitamins							
rs4501570	TTPA	-/-					
rs4606052	TTPA	-/-	Vit E (alpha Tocopherol)				
rs4587328	TTPA	-/-					
rs7501331	BCOM1	+/-	Vitamin A	10,000 units of Vitamin A daily	Recommend Foods High in Vit A	Consider Routine Vitamin A Level	
rs12934922	BCOM1	+/-					
rs11558471	SLC30A8	-/-	Avoid High Dose Zinc				
rs33972313	SLC23A1	-/-	High Dose Vitamin C				

- 36 - Male

(-/-) No clinical abnormality (+/-) Heterozygous result (+/+) Homozygous result

rsID	Gene	Genetic Result	Therapeutics Associated With Positive Result	Highly Recommended Therapeutics	Provider Discretion: As Needed Formula Recommendations	Lifestyle Recommendations	Laboratory Recommendations
rs1395	SLC5A6	-/-	Biotin (B7) and Pantothenate (B5)				
rs6535454	CoQ2	+/+	CoQ-10, PQQ	Mito-Cell PQQ™			Consider Routine CoQ10 level
rs731236	VDR Taq	+/-	Vitamin D				Consider Routine Vitamin D Level
rs2282679	GC or DBP	-/-	Vitamin K		Vitamin D3+K2 (5000 units daily)		
rs1801198	TCN2	+/-	Methyl B12 Adenosyl B12		Methylation Pro Topical™ OR Methylation Complete Fast Dissolves™ once daily		Consider Routine Plasma B12 Level
rs1867277	FOXE1	-/-	Iodine				Consider Routine Thyroid Panel
rs225014	DIO2	+/-	Selenium		Seleniomethionine 200 mcg per day if Free T3 is Low		

Summary for Essential Vitamins

Highly Recommended Therapeutics	Provider Discretion: As Needed Formula Recommendations	Lifestyle Recommendations	Laboratory Recommendations
<ul style="list-style-type: none">• 10,000 units of Vitamin A daily• Mito-Cell PQQ™	<ul style="list-style-type: none">• Vitamin D3+K2 (5000 units daily)• Methylation Pro Topical™ OR Methylation Complete Fast Dissolves™ once daily• Seleniomethionine 200 mcg per day if Free T3 is Low	<ul style="list-style-type: none">• Recommend Foods High in Vit A	<ul style="list-style-type: none">• Consider Routine Vitamin A Level• Consider Routine CoQ10 level• Consider Routine Vitamin D Level• Consider Routine Plasma B12 Level• Consider Routine Thyroid Panel

VITAMIN A

VARIANTS IN THE BCOM1 GENE HAVE BEEN ASSOCIATED WITH DISRUPTED VITAMIN A SYNTHESIS

BENEFITS



Helps maintains healthy teeth, skin and tissues



Has a role in a healthy pregnancy and breastfeeding



Promotes good eyesight



May play a role in cancers, age-related macular degeneration & measles

DEFICIENCY VS HIGH INTAKE

Deficiency

- Risk for eye problems - blindness, night blindness, xerophthalmia (non-reversible corneal damage)
- Hyperkeratosis (dry, scaly skin)
- Diarrhea

High intake

- Birth defects in eyes, skull, lungs and heart
- Acute/Chronic Vitamin A poisoning
 - Dizziness
 - Nausea
 - Headaches
 - Skin irritation
 - Pain in joints and bones
 - Coma
- Increased fracture risk

FOODS HIGH IN VITAMIN A



Meats & fish (beef liver, tuna, herring, salmon, chicken)



Breakfast cereals



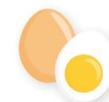
Fruits (oranges, cantaloupe, mangos, apricots)



Black-eyed beans



Dairy products (fat-free or skim milk, part-skim ricotta cheese, low-fat yogurt)



Hard boiled eggs



Vegetables (broccoli, spinach, dark leafy greens, carrots, sweet potatoes, pumpkin, peppers (sweet, red, raw), summer squash)



Pistachios

Gene Information Key

rsID	Gene	"-" variant	"+" variant
rs12934922	BCOM1	A	T
rs7501331	BCOM1	C	T
rs6535454	CoQ2	A	G
rs225014	DIO2	T	C
rs1867277	FOXE1	G	A
rs2282679	GC or DBP	T	G
rs33972313	SLC23A1	C	T
rs11558471	SLC30A8	A	G
rs1395	SLC5A6	G	A
rs1801198	TCN2	C	G
rs4501570	TTPA	A	G
rs4587328	TTPA	C	T
rs4606052	TTPA	C	T
rs731236	VDR Taq	A	G

Definitions

ESSENTIAL VITAMINS	The polymorphisms in this panel will identify any potential weakness of absorption, conversion or delivery or your essential vitamins.
BCOM1 Ala379Val	BCOM1 (?-carotene 15,15?-monoxygenase) converts beta-carotene into retinol (Vit A). Almost half of the population carry significant variants of the BCOM1 gene. There are two genetic variations of the BCOM1 gene which create significant weakness in the conversion to Vit. A. People with a T allele on both rs12934922 and rs7501331 have a 69% decreased conversion of beta-carotene to retinol. For people with only a single T in the rs7501331 SNP, the conversion is decreased by 32%. Vitamin A is a general term that covers several different forms of the vitamin. Animal food sources mainly provide retinyl palmitate, which is broken down in the intestines to retinol. In this form, it is stored by the body and then converted to an active form for use. The plant forms of vitamin A are called carotenes, such as beta-carotene which is found in abundance in carrots and other orange-colored foods. About 80-90% of the retinoids in the body are stored in the liver and used to maintain a steady level in the blood. The body then uses the retinoids in a variety of ways including in stem cells, photoreceptors in the eye, epithelial cells, embryonic cells, various immune cells, red blood cells, and much more.
COQ2	CoQ2 (Para-hydroxybenzoate—polypropenyltransferase, mitochondrial) codes for an enzyme that functions in the final steps in the biosynthesis of CoQ10 (ubiquinone).. This enzyme, which is part of the coenzyme Q10 pathway, catalyzes the prenylation of parahydroxybenzoate with an all-trans polypropenyl group. Mutations in this gene cause coenzyme Q10 deficiency. Polymorphisms in this gene can lead to severe fatigue, muscle weakness, exercise intolerance and general mitochondrial weakness.
GC or DBP	GC aka DBP (Vit. D Binding Protein) gene codes for Vit. D binding protein. This protein belongs to the albumin family and is a multifunctional protein found in plasma, ascitic fluid, cerebrospinal fluid and on the surface of many cell types. It is manufactured in the hepatic parenchymal cells. DBP is capable of binding to all forms of Vit D including ergocalciferol (vitamin D2) and cholecalciferol (vitamin D3), the 25-hydroxylated forms (calcifediol) and the active hormonal product, 1,25-dihydroxyvitamin D (calcitriol). The major proportion of vitamin D in blood is bound to this protein. It transports vitamin D metabolites between skin, liver and kidney, and then on to the various target tissues. It binds to vitamin D and its plasma metabolites and transports them to target tissues. Polymorphisms in this gene decrease the affinity of the protein to Vit. D which reduces the response rate to Vit. D therapy. Patients with these polymorphisms require high doses of Vit D supplementation.
SLC23A1	SLC23A1 (Solute Carrier Family 23A1) codes for an enzyme that functions as a sodium dependent Vit. C transporter. This enzyme functions as one of the two enzymes responsible for the absorption of vitamin C and its distribution to organs in the body. Polymorphisms in this gene have been linked to Vit. C deficiency and additionally to Glaucoma.
SLC30A8	The SLC30A8 (Solute Carrier Family 30A8) polymorphism that codes for a less efficient zinc efflux transporter that can result in the accumulation of zinc in intracellular vesicles. This gene is expressed at a high level in the pancreas and in the macula. Allelic variants of this gene confer susceptibility to diabetes mellitus and poor response to zinc containing supplements for macular degeneration.
SLC5A6	SLC5A6 (Solute Carrier Family 5A6) codes for an enzyme that is responsible for transport of pantothenate (B5) and biotin (B7). This polymorphism can affect both intestinal uptake, cellular delivery and transplacental vitamin transport. Both pantothenate and biotin are very important in the metabolism of fats and carbohydrates, carbon dioxide transport and in gluconeogenesis. Most symptoms of weakness in this enzyme can cause hair loss, skin rash, brittle nails and tingling of the extremities.
TTPA rs4501570	This gene encodes a soluble protein that binds alpha-tocopherol, a form of vitamin E, with high selectivity and affinity. This protein plays an important role in regulating vitamin E levels in the body by transporting vitamin E between membrane vesicles and facilitating the secretion of vitamin E from hepatocytes to circulating lipoproteins. Mutations in this gene cause vitamin E deficiency
HEALTH PRECAUTIONS	
DIO2	DIO1 (Deiodinase 1) codes for an enzyme in the iodothyronine deiodinase family. It catalyzes the activation, as well as the inactivation of thyroid hormone by outer and inner ring deiodination, respectively. Specifically, it is responsible for the selenium-dependent conversion of T4 thyroid to T3 thyroid.
INFLAMMATORY	This Enzyme category has significant effects on the inflammatory state of a person's body. Polymorphisms in these specific enzymes will significantly increase the levels of inflammation in the body. By supplementing these enzyme deficiencies, the patient will effectively reduce inflammatory damage to the body.
VDR Taq1	The Vitamin D (calcitriol) Receptor is a member of the nuclear receptor family. Upon activation by vitamin D (a secosteroid), the VDR causes the activation or deactivation of protein production by the cell. Impaired vitamin D function can result in significant immune weakness and increased cancer risk, as well as, early bone loss, an increased risk of cognitive decline and mood disorders.
METABOLIC RISK FACTOR	The polymorphisms in this category relate to increase risk of developing metabolic syndromes including diabetes, fatty liver, hypothyroidism and insulin resistance.
FOXE1	FOXE1 (Forkhead Box Protein E1) is a gene that codes for a protein that is intimately involved in thyroid hormone synthesis. Polymorphisms in this gene most commonly lead to an increased risk of hypothyroidism due to a weakened ability to synthesize thyroid hormone.
METHYLATION	Methylation is a primary biochemical process in the body that involves the addition of a "methyl" chemical group to a vitamin or neurotransmitter. The addition of the "methyl" group allows for very specific biochemical interactions. Poor "methylation" function alters the effectiveness, delivery and function of many vitamins and important chemicals in the cell.

TCN2

The protein product of the Transcobalamin 2 gene, TCN2, binds the active form of vitamin B-12. Individuals with the G/G phenotype at rs1801198 have decreased serum B-12 and increased homocysteine when compared to individuals with the C/C phenotype.

Disclaimers

TESTING:

Testing Performed By: TY

METHODOLOGY AND LIMITATIONS:

Testing for genetic variation/mutation on listed genes was performed using ProFlex PCR and Real-Time PCR with TaqMan® allele-specific probes on the QuantStudio 12K Flex. All genetic testing is performed by GX Sciences, 4150 Freidrich Lane, Ste H, Austin, TX. 78744. This test will not detect all the known alleles that result in altered or inactive tested genes. This test does not account for all individual variations in the individual tested. Test results do not rule out the possibility that this individual could be a carrier of other mutations/variations not detected by this gene mutation/variation panel. Rare mutations surrounding these alleles may also affect our detection of genetic variations. Thus, the interpretation is given as a probability. Therefore, this genetic information shall be interpreted in conjunction with other clinical findings and familial history for the administration of specific nutrients. Patients should receive appropriate genetic counseling to explain the implications of these test results. Details of assay performance and algorithms leading to clinical recommendations are available upon request. The analytical and performance characteristics of this laboratory developed test (LDT) were determined by GX Sciences' laboratory pursuant to Clinical Laboratory Improvement Amendments (CLIA) requirements.

CLIA #: 45D2144988 Laboratory Director: James Jacobson, PhD

DISCLAIMER:

This test was developed and its performance characteristics determined by GX Sciences. It has not been cleared or approved by the FDA. The laboratory is regulated under CLIA and qualified to perform high-complexity testing. This test is used for clinical purposes. It should not be regarded as investigational or for research. rsIDs for the alleles being tested were obtained from the dbSNP database (Build 142).

DISCLAIMER:

UND Result: If you have received the result Variant undetermined (UND) this indicates that we were not able to determine your carrier status based on your raw data. Please refer to the GX Sciences genetic knowledge database for more information: https://www.gxsciences.com/kb_results.asp

DISCLAIMER:

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GX Sciences SNP References

ESSENTIAL VITAMINS SNP References

BCOM1

- Czecuga-Semeniuk, E. et al. The preliminary association study of ADIPOQ, RBP4, and BCOM1 variants with polycystic ovary syndrome and with biochemical characteristics in a cohort of Polish women. *Advances in Medical Sciences* 63, 242–248 (2018). • Lietz, G., Oxley, A., Leung, W. & Hesketh, J. Single Nucleotide Polymorphisms Upstream Gene Influence Provitamin A Conversion Efficiency in Female Volunteers. *Journal of Nutrition* 142, 161S–165S (2012). • Leung, W. C. et al. Two common single nucleotide polymorphisms in the gene encoding -carotene 15,15'-monooxygenase alter -carotene metabolism in female volunteers. *The FASEB Journal* 23, 1041–1053 (2009). • Office of Dietary Supplements - Vitamin A. NIH Office of Dietary Supplements (2020). Available at: <https://ods.od.nih.gov/factsheets/VitaminA-HealthProfessional/>. • Wax, E. & Conaway, B. Vitamin A: MedlinePlus Medical Encyclopedia. MedlinePlus (2019). Available at: <https://medlineplus.gov/ency/article/002400.htm>. • Beydoun, M. A., Nalls, M. A., Canas, J. A., Evans, M. K. & Zonderman, A. B. Gene polymorphisms and gene scores linked to low serum carotenoid status and their associations with metabolic disturbance and depressive symptoms in African-American adults. *British Journal of Nutrition* 112, 992–1003 (2014). • Borel, P., De Edelenyi, F. S., Vincent-Baudry, S., Malezet-Desmoulin, C., Margotat, A., Lyan, B., ... Bieuvet, S. (2011). Genetic variants in BCOM1 and CD36 are associated with plasma lutein concentrations and macular pigment optical density in humans. *Annals of Medicine*, 43(1), 47–59.

CoQ2

- Turunen, M., Olsson J., Dallner G.. Metabolism and function of coenzyme Q. *Biochem. Biophys. Acta* , 2004, vol. 1660 (pg. 171-199) • Santos-Ocana C., Do T.Q., Padilla S., Navas P., Clarke C.F.. Uptake of exogenous coenzyme Q and transport to mitochondria is required for bc1 complex sustainability in yeast coq mutants. *J. Biol. Chem.*, 2002, vol. 277 (pg. 10973-10981) • Oh, J., Ban, M. R., Miskie, B. A., Pollex, R. L., & Hegele, R. A. (2007). Genetic determinants of statin intolerance. *Lipids in Health and Disease*, 6. <https://doi.org/10.1186/1476-511X-6-7> • López-Martin, J. M., Salvati, L., Trevisson, E., Montini, G., DiMauro, S., Quinzii, C., ... Navas, P. (2007). Missense mutation of the COQ2 gene causes defects of bioenergetics and de novo pyrimidine synthesis. *Human Molecular Genetics*, 16(9), 1091–1097. <https://doi.org/10.1093/hmg/ddm058> • Jakobs, B. S., Van Den Heuvel, L. P., Smets, R. J. P., De Vries, M. C., Hien, S., Schaible, T., Rodenburg, R. J. T. (2013). A novel mutation in COQ2 leading to fatal infantile multisystem disease. *Journal of the Neurological Sciences*, 326(1–2), 24–28. <https://doi.org/10.1016/j.jns.2013.01.004> • Hubacek, J. A., Adamkova, V., Zlatohlavek, L., Steiner-Mrazova, L., & Vrablik, M. (2017). COQ2 polymorphisms are not associated with increased risk of statin-induced myalgia/myopathy in the Czech population. *Drug Metabolism and Personalized Therapy*, 32(4), 177–182. <https://doi.org/10.1515/dmpt-2017-0027> • Diomed-Carnasselli, F., Di Giandomenico, S., Santorelli, F. M., Caridi, G., Piemonte, F., Montini, G., Emma, F. (2007). COQ2 Nephropathy: A Newly Described Inherited Mitochondriopathy with Primary Renal Involvement. *Journal of the American Society of Nephrology*, 18(10), 2773–2780. <https://doi.org/10.1016/j.jasn.2009.06.001> • MitoQ. Which Foods Help Your Mitochondria? MitoQ (2019). Available at: [### GC or DBP](https://www.mitoq.com/blog/which-foods-help-your-mitochondria#:~:text=Simple carbohydrates like white flour,efficient,long-lasting way.~*West, A. P., Shadel, G. S. & Ghosh, S. Mitochondria in innate immune responses. <i>Nature Reviews Immunology</i> (2011). doi:10.1038/nri2975 • Friedman, J. R. & Nunnari, J. Mitochondrial form and function. <i>Nature</i> (2014). doi:10.1038/nature12985 • Kann, O. & Kovács, R. Mitochondria and neuronal activity. <i>American Journal of Physiology - Cell Physiology</i> (2007). doi:10.1152/ajpcell.00222.2006 • Pizzorno, J. Mitochondria-fundamental to life and health. <i>Integrative Medicine</i> (Boulder) (2014).</div><div data-bbox=)

- Slater, N. A., Rager, M. L., Havrda, D. E. & Harralson, A. F. Genetic Variation in CYP2R1 and GC Genes Associated with Vitamin D Deficiency Status. *Journal of Pharmacy Practice* 30, 31–36 (2017). • Hill, A. How to Get Vitamin D: 7 Effective Ways. *Healthline* (2019). Available at: <https://www.healthline.com/nutrition/how-to-increase-vitamin-d>. • Database, G. C. H. G. GC Gene (Protein Coding). *GeneCards* Available at: <https://www.genecards.org/cgi-bin/cardisp.pl?gene=GC>. • Cheung, C. L., Lau, K. S., Sham, P. C., Tan, K. C. & Kung, A. W. Genetic variant in vitamin D binding protein is associated with serum 25-hydroxyvitamin D and vitamin D insufficiency in southern Chinese. *Journal of Human Genetics* 58, 749–751 (2013). • Davies, J. R., Field, S., Randerson-Moor, J., Harland, M., Kumar, R., Anic, G. M., ... Newton-Bishop, J. (2014). An inherited variant in the gene coding for vitamin D-binding protein and survival from cutaneous melanoma: A BioGenoMEL study. *Pigment Cell and Melanoma Research*. <https://doi.org/10.1111/pcmr.12193> • Elkum, N., Alkayal, F., Noronha, F., Ali, M. M., Melhem, M., Al-Arouj, M., ... Abubaker, J. (2014). Vitamin D insufficiency in Arabs and South Asians positively associates with polymorphisms in GC and CYP2R1 genes. *PLoS ONE*. <https://doi.org/10.1371/journal.pone.0113102> • Leong, A., Rehman, W., Dastani, Z., Greenwood, C., Timpson, N., Langsetmo, L., ... Richards, J. B. (2014). The Causal Effect of Vitamin D Binding Protein (DBP) Levels on Calcemic and Cardiometabolic Diseases: A Mendelian Randomization Study. *PLoS Medicine*. <https://doi.org/10.1371/journal.pmed.1001751> • Nimithipong, Hataikarn, Chanika Srirata, La Orahilurkit, Suwannee Chanprasertyothin, Wipa Ratanachawong, Piyamit Srirata, and Boonsong Onghiphadhanakul. 2015. "Relationship of Vitamin D Status and Bone Mass According to Vitamin D-Binding Protein Genotypes." *Nutrition Journal* 14 (1). BioMed Central Ltd. doi:10.1186/s12937-015-0016-1. • Szkandera, J. et al. Association of common gene variants in vitamin D modulating genes and colon cancer recurrence. *Journal of Cancer Research and Clinical Oncology* 139, 1457–1464 (2013). • Theodoratou, E., Palmer, T., Zgaga, L., Farrington, S. M., McKeigue, P., Din, F. V. N., ... Campbell, H. (2012). Instrumental variable estimation of the causal effect of plasma 25-hydroxyvitamin D on colorectal cancer risk: A Mendelian randomization analysis. *PLoS ONE*. <https://doi.org/10.1371/journal.pone.0037662> • Trummer, O., Langsenlehner, U., Krenn-Pilko, S., Pieber, T. R., Obermayer-Pietsch, B., Gerger, A., Langsenlehner, T. (2016). Vitamin D and prostate cancer prognosis: a Mendelian randomization study. *World Journal of Urology*. <https://doi.org/10.1007/s00435-015-1646-9> • Wang, W., Ingles, S. A., Torres-Mejia, G., Stern, M. C., Stanczyk, F. Z., Schwartz, G. G., ... John, E. M. (2014). Genetic variants and non-genetic factors predict circulating vitamin D levels in Hispanic and non-Hispanic White women: The breast cancer health disparities study. *International Journal of Molecular Epidemiology and Genetics*. • Wang, Y., Wang, O., Li, W., Ma, L., Ping, F., Chen, L., & Nie, M. (2015). Variants in Vitamin D binding protein gene are associated with gestational diabetes mellitus. *Medicine* (United States). <https://doi.org/10.1097/MD.00000000000001693>

SLC23A1

- Duell, E. J., Lujan-Barroso, L., Llivina, C., Muñoz, X., Jenab, M., Boutron-Ruault, M. C., ... González, C. A. (2013). Vitamin C transporter gene (SLC23A1 and SLC23A2) polymorphisms, plasma vitamin C levels, and gastric cancer risk in the EPIC cohort. *Genes and Nutrition*. <https://doi.org/10.1007/s12263-013-0346-6> • Shaghaghi, M. A., Bernstein, C. N., León, A. S., El-Gabalawy, H., & Eck, P. (2014). Polymorphisms in the sodium-dependent ascorbate transporter gene SLC23A1 are associated with susceptibility to Crohn disease-1. *American Journal of Clinical Nutrition*. <https://doi.org/10.3945/ajcn.113.068015> • Timpson, N. J., Forouhi, N. G., Brion, M. J., Harbord, R. M., Cook, D. G., Johnson, P., ... Smith, G. D. (2010). Genetic variation at the SLC23A1 locus is associated with circulating concentrations of L-ascorbic acid (vitamin C): Evidence from 5 independent studies with >15,000 participants. *American Journal of Clinical Nutrition*. <https://doi.org/10.3945/ajcn.2010.29438> • Wade, K. H., Forouhi, N. G., Cook, D. G., Johnson, P., McConnachie, A., Morris, R. W., ... Timpson, N. J. (2015). Variation in the SLC23A1 gene does not influence cardiometabolic outcomes to the extent expected given its association with L-ascorbic acid. *American Journal of Clinical Nutrition*. <https://doi.org/10.3945/ajcn.114.092981> • Zheng, F., JuWen, J., & Hong, Y. (2018). Study on the correlation between vitamin E level and preeclampsia in pregnant women. *Maternal and Child Health Care of China*.

SLC30A8

- Lin, Y., Li, P., Cai, L., Zhang, B., Tang, X., Zhang, X., ... Yang, Z. (2010). Association study of genetic variants in eight genes/loci with type 2 diabetes in a Han Chinese population. *BMC Medical Genetics*. <https://doi.org/10.1186/1471-2350-11-97> • Rees, S. D., Hydrie, M. Z. I., O'Hare, J. P., Kumar, S., Shera, A. S., Basit, A., ... Kelly, M. A. (2011). Effects of 16 genetic variants on fasting glucose and type 2 diabetes in South Asians: ADCY5 and GLIS3 variants may predispose to type 2 diabetes. *PLoS ONE*. <https://doi.org/10.1371/journal.pone.0024710> • Xu, J., Wang, J., & Chen, B. (2012). SLC30A8 (ZnT8) variations and type 2 diabetes in the Chinese Han population. *Genetics and Molecular Research*. <https://doi.org/10.4238/2012.May.24.1> • National Institutes of Health. Foods Without Zinc. Foods without Zinc Available at: <http://dietgrail.com/no-zinc-foods/> • Abu Seman, N., Wan Mohamud, W. N., Ostenson, C. G., Brismar, K., & Gu, H. F. (2015). Increased dna methylation of the slc30a8 gene promoter is associated with type 2 diabetes in a malay population. *Clinical Epigenetics*. <https://doi.org/10.1186/s13148-015-0049-5> • Fu, L., Lin, Y., Yang, Z. L., & Yin, Y. B. (2012). Association analysis of genetic polymorphisms of TCF7L2, CDKAL1, SLC30A8, HHEX genes and microvascular complications of type 2 diabetes mellitus. *Chinese Journal of Medical Genetics*. <https://doi.org/10.3760/cma.j.issn.1003-9406.2012.02.017> • Kanoni, S., Nettleton, J. A., Hivert, M. F., Ye, Z., Van Rooij, F. J. A., Shungin, D., ... Dedousis, G. V. (2011). Total zinc intake may modify the glucose-raising effect of a zinc transporter (SLC30A8) variant: A 14-cohort meta-analysis. *Diabetes*. <https://doi.org/10.2337/db11-0176> • J., H. et al. Genetic variants associated with type 2 diabetes and obesity better predict gestational diabetes than traditional risk factors. *Diabetologia* 57, S448 (2014). • Wax, E. & Conaway, B. Zinc in diet: MedlinePlus Medical Encyclopedia. MedlinePlus (2019). Available at: <https://medlineplus.gov/ency/article/002416.htm> • Office of Dietary Supplements - Zinc. NIH Office of Dietary Supplements (2020). Available at: <https://ods.od.nih.gov/factsheets/Zinc-HealthProfessional/>.

SLC5A6

- Prasada PD, Wang H, Huang W, Fei YJ, Leibach FH, Devoe LD, Ganapathy V. Molecular and functional characterization of the intestinal Na+-dependent multivitamin transporter. *Arch Biochem Biophys* 366: 96-106, 1999. • Said HM. Cell and molecular aspects of human intestinal biotin absorption. *J Nutr* 139: 158-162, 2009. • Sabui, S., J., Kapadia, R., Cogburn, K., Ghosal, A., Lambrecht, N. W., & Said, H. M. (2016). Role of the sodium-dependent multivitamin transporter (SMVT) in the maintenance of intestinal mucosal integrity. *American Journal of Physiology-Gastrointestinal and Liver Physiology*, 311(3), G561–G570. <https://doi.org/10.1152/ajpgi.00240.2016> • Süssing, T. M., Deeken, J., Leibbrand, C. R., Price, D. K., Ehrlich, S., Steinberg, S. M., ... Figg, W. D. (2016). Identification of novel SNPs associated with risk and prognosis in patients with castration-resistant prostate cancer. *Pharmacogenomics*. <https://doi.org/10.2217/pgs-2016-0134> • Subramanian, V. S., Constantinescu, A. R., Benke, P. J., & Said, H. M. (2017). Mutations in SLC5A6 associated with brain, immune, bone, and intestinal dysfunction in a young child. *Human Genetics*, 136(2), 253–261. <https://doi.org/10.1007/s00439-016-1751-x> • Wolf B. Disorders of biotin metabolism. *The Metabolic and Molecular Bases of Inherited Disease* New York McGraw-Hill 3935-3962, 2001. • Ghosal, A., & Said, H. M. (2011). Structure-function activity of the human sodium-dependent multivitamin transporter: role of His115&His254. *American Journal of Physiology, Cell Physiology*, 300(1), C97–C104. <https://doi.org/10.1152/ajpcell.00398.2010> • Mock D. Biotin: Physiology, dietary Sources and Requirements London Academic 2004. • Office of Dietary Supplements - Pantothenic Acid. NIH Office of Dietary Supplements (2020). Available at: <https://ods.od.nih.gov/factsheets/PantothenicAcid-HealthProfessional/>. • Office of Dietary Supplements - Biotin. NIH Office of Dietary Supplements (2020). Available at: <https://ods.od.nih.gov/factsheets/Biotin-HealthProfessional/>. • Wax, E. & Conaway, B. Pantothenic acid and biotin: MedlinePlus Medical Encyclopedia. MedlinePlus (2020). Available at: <https://medlineplus.gov/ency/article/002410.htm>.

TTPA

HEALTH PRECAUTIONS SNP References

FOXE1

- Genetic Predisposition to Papillary Thyroid Carcinoma: Involvement of FOXE1, TSHR, and a Novel lincRNA Gene, PTCSC2 Huiling He, Wei Li, Sandya Liyanarachchi, Jaroslaw Jendrzejewski, Mukund Srinivas, Ramana V. Davuluri, Rebecca Nagy, Albert de la Chapelle J Clin Endocrinol Metab. 2015 Jan; 100(1): E164–E172. Published online 2014 Oct 10. doi: 10.1210/jc.2014-2147 • Variants Near FOXE1 Are Associated with Hypothyroidism and Other Thyroid Conditions: Using Electronic Medical Records for Genome- and Phenome-wide Studies Joshua C. Denny, Dana C. Crawford, Marylyn D. Ritchie, Suzette J. Bielinski, Melissa A. Basford, Yuki Bradford, High Seng Chai, Lisa Bastarache, Rebecca Zuvich, Peggy Peissig, David Carroll, Andrea H. Ramirez, Jyothishman Pathak, Russell A. Wilke, Luke Rasmussen, Xiaoming Wang, Jennifer A. Pacheco, Abel N. Kho, M. Geoffrey Hayes, Noah Weston, Martha Matsumoto, Peter A. Kopp, Katherine M. Newton, Gail P. Jarvik, Rongling Li, Teri A. Manolio, Itzhak J. Kullo, Christopher G. Chute, Rex L. Chisholm, Eric B. Larson, Catherine A. McCarty, Daniel R. Matsys, Dan M. Roden, Mariza de Andrade Am J Hum Genet. 2011 Oct 7; 89(4): 529–542. doi: 10.1016/j.ajhg.2011.09.008 • Multiple functional variants in long-range enhancer elements contribute to the risk of SNP rs965513 in thyroid cancer Huiling He, Wei Li, Sandya Liyanarachchi, Mukund Srinivas, Yanqiang Wang, Keiko Akagi, Yao Wang, Dayong Wu, Qianben Wang, Victor Jin, David E. Symer, Rulong Shen, John Phay, Rebecca Nagy, Albert de la Chapelle Proc Natl Acad Sci U S A. 2015 May 12; 112(19): 6126–6133. Published online 2015 Apr 27. doi: 10.1073/pnas.1506255112 • Genetic associations with neonatal thyroid stimulating hormone levels Farah Y. Alul, Oleg A. Shchelochkov, Stanton L. Berberich, Jeffrey C. Murray, Kelli K. Ryckman Pediatr Res. 2013 Apr; 73(4 0 1): 484–491. Published online 2013 Jan 23. doi: 10.1038/pr.2013.18 • Novel Genetic Loci Identified for the Pathophysiology of Childhood Obesity in the Hispanic Population Anthony G. Comuzzie, Shelley A. Cole, Sandra L. Laston, V. Saroja Voruganti, Karin Haack, Richard A. Gibbs, Nancy F. Butler PLoS One. 2012; 7(12): e51954. Published online 2012 Dec 14. doi: 10.1371/journal.pone.0051954 • The Variant rs1867277 FOXE1 Gene Confers Thyroid Cancer Susceptibility through the Recruitment of USF1/USF2 Transcription Factors Iñigo Landa, Sergio Ruiz-Llorente, Cristina Montero-Conde, Lucía Ingla-Pérez, Francesca Schiavi, Susanna Leskela, Guillermo Pita, Roger Milne, Javier Maravall, Ignacio Ramos, Victor Andia, Paloma Rodríguez-Poyó, Antonio Jara-Albarrán, Amparo Meiro, Cristina del Peso, Luis Arribas, Pedro Iglesias, Javier Caballero, Joaquín Serrano, Antonio Picó, Francisco Pomares, Gabriel Giménez, Pedro López-Mondejar, Roberto Castello, Isabella Merante-Boschin, María-Rosa Pelizzio, Didac Mauricio, Giuseppe Opocher, Cristina Rodríguez-Antón, Anna González-Neira, Xavier Matías-Guiu, Pilar Santisteban, Mercedes Robledo PLoS Genet. 2009 Sep; 5(9): e1000637. Published online 2009 Sep 4. doi: 10.1371/journal.pgen.1000637 • Quantitative Assessment of Common Genetic Variants on FOXE1 and Differentiated Thyroid Cancer Risk Hongling Zhu, Qian Xi, Liangyong Liu, Jingnan Wang, Mingjun Gu PLoS One. 2014; 9(1): e87332. Published online 2014 Jan 29. doi: 10.1371/journal.pone.0087332 • Patterns of FOXE1 Expression in Papillary Thyroid Carcinoma by Immunohistochemistry Andrey Bychkov, Vladimir Saenko, Masahiro Nakashima, Norisato Mitsutake, Tatiana Rogounovitch, Alyaksandr Nikitski, Florence Orim, Shunichi Yamashita Thyroid. 2013 Jul; 23(7): 817–828. doi: 10.1089/thy.2012.0466 • The investigation of foxe1 variations in papillary thyroid carcinoma Erkan Somuncu, Adem Karatas, Sinan Ferahman, Neslihan Saygili, Eren Yilmaz, Oguz Ozturk, Metin Kapan Int J Clin Exp Pathol. 2015; 8(10): 13458–13464. Published online 2015 Oct 1. • FOXE1 Association with Differentiated Thyroid Cancer and Its Progression Marissa Penna-Martinez, Friederike Epp, Heinrich Kahles, Elizabeth Ramos-Lopez, Nora Hirsch, Martin-Leo Hansmann, Ivan Selkinski, Frank Grünwald, Katharina Holzer, Wolf O. Bechstein, Stefan Zeuzem, Christian Vorländer, Klaus Badenhoop Thyroid. 2014 May 1; 24(5): 845–851. doi: 10.1089/thy.2013.20274

INFLAMMATORY SNP References

VDRTaq

- Adorini, L., Daniel, K. & Penna, G. Vitamin D Receptor Agonists, Cancer and the Immune System: An Intricate Relationship. *Curr. Top. Med. Chem.* (2006). doi:10.2174/156802606777864890 • McKenna, M. J. & Murray, B. Vitamin D deficiency, in Endocrinology and Diabetes: A Problem-Oriented Approach (2014). doi:10.1007/978-1-614-8684-8_23 • Fischer, K. Vitamin D in Principles of Nutrigenetics and Nutrigenomics: Fundamentals of Individualized Nutrition (2019). doi:10.1016/B978-0-12-804572-5.00032-X • Bikle, D. D. Vitamin D metabolism, mechanism of action, and clinical applications. *Chemistry and Biology* (2014). doi:10.1016/j.chembiol.2013.12.016 • Cielsińska, A. et al. Vitamin D receptor gene polymorphisms associated with childhood autism. *Brain Sci.* (2017). doi:10.3390/brainsci7090115 • Kamel, M. M., Fouad, S. A., Salaheldin, O., El-Razek, A. E. R. A. A. & El-Fatah, A. I. A. Impact of vitamin D receptor gene polymorphisms in pathogenesis of Type-1 diabetes mellitus. *Int. J. Clin. Exp. Med.* (2014). • El-Shal, A. S., Shalaby, S. M., Aly, N. M., Rashad, N. M. & Abdelaziz, A. M. Genetic variation in the vitamin D receptor gene and vitamin D serum levels in Egyptian women with polycystic ovary syndrome. *Mol. Biol. Rep.* (2013). doi:10.1007/s11033-013-2716-y • Keen, R. W., Hart, D. J., Lanchbury, J. S. & Spector, T. D. Association of early, osteoarthritis of the knee with a Taq I polymorphism of the vitamin D receptor gene. *Arthritis Rheum.* (1997). doi:10.1002/art.1780400812 • Kyung, S. P., Jung, H. N. & Choi, J. The short vitamin D receptor is associated with increased risk for generalized aggressive periodontitis. *J. Clin. Periodontol.* (2006). doi:10.1111/j.1600-051X.2006.00944.x • Wang, Y. et al. Variants in Vitamin D binding protein gene are associated with gestational diabetes mellitus. *Med. (United States)* (2015). doi:10.1097/MD.00000000000001693 • Hill, A. How to Get Vitamin D: 7 Effective Ways. *Healthline* (2019). Available at: <https://www.healthline.com/nutrition/how-to-increase-vitamin-d> • Baudino, T. A. et al. Isolation and characterization of a novel coactivator protein, NCoA-62, involved in vitamin D-mediated transcription. *J. Biol. Chem.* (1998). doi:10.1074/jbc.273.26.16434 • Lisse, T. S., Chun, R. F., Rieger, S., Adams, J. S. & Hewison, M. Vitamin D activation of functionally distinct regulatory miRNAs in primary human osteoblasts. *J. Bone Miner. Res.* (2013). doi:10.1002/jbm.1882 • Fleet, J. C. & Schoch, R. D. Molecular mechanisms for regulation of intestinal calcium and phosphate absorption by vitamin D in Vitamin D (2011). doi:10.1016/B978-0-12-381978-9.10019-8 • Germain, P., Staels, B., Daquet, C., Spedding, M. & Laudet, V. Overview of Nomenclature of Nuclear Receptors. *Pharmacol. Rev.* (2006). doi:10.1124/pr.58.2 • Tagami, T., Lutz, W. H., Kumar, R. & Jameson, J. L. The interaction of the vitamin D receptor with nuclear receptor corepressors and coactivators. *Biochem. Biophys. Res. Commun.* (1998). doi:10.1006/bbrc.1998.9799 • Hérdick, M., Steinmyer, A. & Carlerig, C. Antagonistic action of a 25-carboxylic ester analogue of 17?,25-dihydroxyvitamin D3 is mediated by a lack of ligand-induced vitamin D receptor interaction with coactivators. *J. Biol. Chem.* (2000). doi:10.1074/jbc.M910000199 • Luderer, H. F. & Demay, M. B. The vitamin D receptor, the skin and stem cells. *J. Steroid Biochem. Mol. Biol.* (2010). doi:10.1016/j.jsbmb.2010.01.015 • Vdr vitamin D (1,25-dihydroxyvitamin D3) receptor [Mus musculus (house mouse)] - Gene - NCBI. National Center for Biotechnology Information (2018). Available at: <https://www.ncbi.nlm.nih.gov/gene/22337>.

METHYLATION SNP References

TCN2

- Regec, A., Quadros, E. V., Platica, O. & Rothenberg, S. P. The cloning and characterization of the human transcobalamin II gene. *Blood* (1995). • Linnebank, M. et al. Association of transcobalamin c. 776C>G with overall survival in patients with primary central nervous system lymphoma. *Br. J. Cancer* (2012). doi:10.1038/bjc.2012.476 • Martinelli, M. et al. A candidate gene study of one-carbon metabolism pathway genes and colorectal cancer risk. *Br. J. Nutr.* (2013). doi:10.1017/S0007114512002796 • Moore, L. D., Le, T. & Fan, G. DNA methylation and its basic function. *Neuropsychopharmacology* (2013). doi:10.1038/npp.2012.112 • Tanaka, T. et al. Genome-wide Association Study of Vitamin B6, Vitamin B12, Folate, and Homocysteine Blood Concentrations. *Am. J. Hum. Genet.* (2009). doi:10.1016/j.ajhg.2009.02.011 • Koushik, A. et al. Nonsynonymous polymorphisms in genes in the one-carbon metabolism pathway and associations with colorectal cancer. *Cancer Epidemiol. Biomarkers Prev.* (2006). doi:10.1158/1055-9965.EPI-06-0624 • Semencz, A. Top 12 Foods That Are High in Vitamin B12. *Healthline* (2020). Available at: <https://www.healthline.com/health/vitamin-b12-foods#10-natural-milk> • Mills, J. L. et al. Folate-related genes and omphalocele. *Am. J. Med. Genet.* (2005). doi:10.1002/ajmg.a.30772 • Martinelli, M. et al. Idiopathic pulmonary fibrosis and polymorphisms of the folate pathway genes. *Clin. Biochem.* (2013). doi:10.1016/j.clinbiochem.2012.10.009 • Office of Dietary Supplements - Vitamin B12. NIH Office of Dietary Supplements (2020). Available at: <https://ods.od.nih.gov/factsheets/VitaminB12-HealthProfessional/#:~:text=Vitamin%20B12%20is%20naturally%20found,5%2C13%2D15%5D> • Miller, A. L. The methionine-homocysteine cycle and its effects on cognitive diseases. *Alternative Medicine Review* (2003). • Teplitsky, V. et al. Hereditary partial transcobalamin II deficiency with neurologic, mental and hematologic abnormalities in children and adults. *Isr. Med. Assoc. J.* (2003). • Refsum, H., Johnston, C., Guttormsen, A. B. & Nexo, E. Holotranscobalamin and total transcobalamin in human plasma: Determination, determinants, and reference values in healthy adults. *Clin. Chem.* (2006). doi:10.1373/clinchem.2005.054619 • Seetharam, B., Bose, S. & Li, N. Cellular Import of Cobalamin (Vitamin B-12) 1,2. *J. Nutr.* (1999). • Winkelmayer, W. C., Skoupy, S., Eberle, C., Födinger, M. & Sunder-Plassmann, G. Effects of TCN2 776C>G on vitamin B, folate, and total homocysteine levels in kidney transplant patients. *Kidney International* (2004). Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC15086930/> • Hoffbrand, A. V., Tripp, E., Jackson, B. F., Luck, W. E. & Frater-Schröder, M. N. Hereditary Abnormal Transcobalamin II Previously Diagnosed as Congenital Dihydrofolate Reductase Deficiency. *New England Journal of Medicine* 310, 789–790 (1984). • Garg, G. et al. Polymorphisms in transcobalamin II gene is associated with coronary artery disease in Indian population. *Biomarkers* (2012). doi:10.3109/1354750X.2011.642408 • Cascalheira, J. F. et al. Association of the transcobalamin II gene 776C>G polymorphism with Alzheimer's type dementia: dependence on the 5, 10-methylenetetrahydrofolate reductase 1298A>C polymorphism genotype. *Ann. Clin. Biochem.* (2015). doi:10.1177/0004563214561770

NEUROTRANSMITTER SNP References

DIO2

- Williams, G. R., & Bassett, J. H. D. (2011). Local control of thyroid hormone action: Role of type 2 deiodinase. *Journal of Endocrinology*. <https://doi.org/10.1530/JOE-10-0448> • Dumitrescu, A. M., Liao, X. H., Abdullah, M. S. Y., Lado-Abeal, J., Majed, F. A., Moeller, L. C., ... Refetoff, S. (2005). Mutations in SECISBP2 result in abnormal thyroid hormone metabolism. *Nature Genetics*. <https://doi.org/10.1038/ng1654> • De Jesus, L. A., Carvalho, S. D., Ribeiro, M. O., Schneider, M., Kim, S. W., Harney, J. W., ... Bianco, A. C. (2001). The type 2 iodothyronine deiodinase is essential for adaptive thermogenesis in brown adipose tissue. *Journal of Clinical Investigation*. <https://doi.org/10.1172/JCI200113803> • Bomer, N., Den Hollander, W., Ramos, Y. F. M., Bos, S. D., Van Der Breggen, R., Lakenberg, N., ... Meulenbelt, I. (2015). Underlying molecular mechanisms of DIO2 susceptibility in symptomatic osteoarthritis. *Annals of the Rheumatic Diseases*. <https://doi.org/10.1136/annrheumdis-2013-204739> • Ma, S. F., Xie, L., Pino-Yanes, M., Sammani, S., Wade, M. S., Letsiou, E., ... Garcia, J. G. N. (2011). Type 2 deiodinase and host responses of sepsis and acute lung injury. *American Journal of Respiratory Cell and Molecular Biology*. <https://doi.org/10.1165/cmb.2011-0179OC>