



Genetic Biosciences For Improving the Quality of Life.

Healthy Aging Assessment For: _____

Bar Code #: _____

What Does GeneLink’s Healthy Aging DNA Assessment Measure?

GeneLink’s Healthy Aging DNA Assessment looks for variations (SNPs) in 12 key genes that are very important in your body’s overall health: specifically your genetic propensity for: Oxidative stress; Environmental challenges; Cardiovascular health; Detoxification; Immune health; Neurological health: Pulmonary health, Eye/Vision health & Bone health.

Understanding SNPs

Small variations in DNA, called single nucleotide polymorphisms, or SNPs (pronounced “snips”), account for all human genetic differences — including how efficient we are at key biological processes. The GeneLink scientific and medical advisory board has developed tests for 12 different SNPs that are known to have an impact on the functioning of the body and that may lead to diminished health and wellness.

Gene Analyzed	General Description	Recommended Support Level
<p>SNP: VDR (Vitamin D Receptor)</p>	<p>The strength of our bones is influenced by the VDR gene. In fact, among healthy people, this one gene accounts for 75% of the entire genetic influence on bone density.ⁱ People with SNPs in the VDR gene tend to have lower bone mineral density than those without these variations.^{ii,iii,iv} SNPs in this gene may also influence young adult growth,^v parathyroid hormone production,^{vi} normal cell division,^{vii} and blood sugar regulation.⁷</p>	<p style="background-color: #008000; color: white; text-align: center; padding: 2px;">Optimum Genetic Function</p> <p style="text-align: center; padding: 5px;">- -</p>
<p>SNP: EPHX (Microsomal Epoxide Hydrolase)</p>	<p>Epoxides are toxic, highly reactive foreign chemicals present in cigarette smoke, car exhaust, charcoal-grilled meat, and smoke from burning wood, pesticides, and alcohol. The body’s way of dealing with epoxides is through the enzyme microsomal EPHX, which detoxifies these foreign compounds. Due to a SNP on the EPHX gene, people with lowered EPHX activity will have difficulty detoxifying harmful substances and thus be particularly vulnerable to their effects.^{viii}</p>	<p style="background-color: #ffff00; text-align: center; padding: 2px;">ADDED SUPPORT</p> <p style="text-align: center; padding: 5px;">+ -</p>
<p>SNP: NQO1 (Coenzyme Q10 Reductase)</p>	<p>Free radicals are considered by many scientists to be the primary cause of aging. The coenzyme Q10 reductase (NQO1) enzyme converts coenzyme Q10 (ubiquinone) to its reduced form, ubiquinol, which scavenges free radicals in the mitochondria and lipid membranes.^{ix} Some individuals have a SNP in the NQO1 gene that slows the reduction of ubiquinone to ubiquinol, resulting in very low blood levels of this key antioxidant. Consequently, people with this SNP are at high risk of free radical attack.^x Because NQO1 is also involved in the detoxification of compounds foreign to the body, a SNP in the NQO1 gene may cause aberrant cellular changes.</p>	<p style="background-color: #ff0000; color: white; text-align: center; padding: 2px;">MAXIMUM SUPPORT</p> <p style="text-align: center; padding: 5px;">+ +</p>
<p>SNP: SOD2 (Manganese Superoxide Dismutase)</p>	<p>The SOD2 enzyme is also involved in scavenging free radicals. However, SOD2 is focused on one particularly toxic type of free radical: superoxide.^{xi} Since the superoxide radical is produced in abundance in all cells, it is the starting point for the free radical chain of production. SOD2 has the distinction of being the only enzyme in the mitochondria that can neutralize superoxide.^{xii} Individuals with a SNP in this gene therefore have a weak first line of defense against free radicals.</p>	<p style="background-color: #ff0000; color: white; text-align: center; padding: 2px;">MAXIMUM SUPPORT</p> <p style="text-align: center; padding: 5px;">+ +</p>
<p>SNP: GPX1 (Glutathione Peroxidase 1)</p>	<p>The GPX1 antioxidant enzyme specifically scavenges hydrogen peroxide, a reactive oxygen species. GPX1 is a selenoprotein, meaning it incorporates selenium into its protein structure.^{xiii} Therefore, how much GPX1 a person produces is dependent on their selenium level.¹³ A SNP on the GPX1 gene can reduce a person’s ability to utilize selenium.^{xiv,xv} That means higher-than-normal selenium intake is needed to afford protection to hydrogen peroxide-sensitive tissues, particularly lung and breast tissues.^{14,xvi,xvii}</p>	<p style="background-color: #008000; color: white; text-align: center; padding: 2px;">Optimum Genetic Function</p> <p style="text-align: center; padding: 5px;">- -</p>
<p>SNP: MMP-1 (Matrix Metalloproteinase)</p>	<p>Collagen is the main component of cartilage, ligaments, tendons, and bone. It is constantly synthesized and broken down in an on-going cycle. MMP1, also known as collagenase, is an enzyme that degrades collagen. People with a SNP in the MMP1 gene produce collagenase at an increased rate, which means their bodies may break down collagen faster than they can rebuild it.^{xviii,xix} These individuals will likely benefit from added support for collagen-rich structures such as the bones and joints.</p>	<p style="background-color: #008000; color: white; text-align: center; padding: 2px;">Optimum Genetic Function</p> <p style="text-align: center; padding: 5px;">- -</p>

Gene Analyzed	General Description	Recommended Support Level
SNP: MTRR (Methionine Synthase Reductase)	Homocysteine is a metabolite of the amino acid methionine. Research has shown it is important to control homocysteine levels in order to preserve cardiovascular health. ^{xx,xxi,xxii} One of the body's methods for keeping homocysteine levels in check is the MTRR enzyme, which transforms homocysteine back to either methionine or cysteine. ^{xxiii} When an individual has a SNP in the MTRR gene, their ability to clear homocysteine from the blood may be hindered. However, only certain population groups appear to be negatively affected by this SNP. ^{23,xxiv,xxv}	ADDED SUPPORT + -
SNP: MTHFR (Methylene Tetrahydrofolate Reductase)	Like the MTRR enzyme, the MTHFR enzyme is responsible for reducing blood levels of homocysteine. People with a SNP in the MTHFR gene manufacture defective enzymes that can't clear homocysteine from the blood efficiently. Research has shown there is a direct association between a SNP in the MRHFR gene and elevated levels of homocysteine, ^{xxvi} particularly in those with low levels of folate. ^{xxvii}	MAXIMUM SUPPORT + +
SNP: TNF-<u> </u> (Tumor Necrosis Factor - <u> </u>)	Inflammation is a response of the immune system to a perceived attack. While it is a helpful response in the short-term, if inflammation continues on-going, it can negatively affect the cells, tissues, and ultimately, the organs. TNF- <u> </u> is a cytokine (a chemical messenger of the immune system) that plays a role in inflammatory processes. Individuals with a SNP on the TNF- <u> </u> gene may have an over-reactive inflammation mechanism, which can negatively affect the joints, ^{xxviii} brain, ^{xxix} lungs, ^{xxx} and heart. ^{xxxi}	Optimum Genetic Function - -
SNP: PON-1 (Paraoxonase 1)	While it used to be thought that high cholesterol posed a health issue in and of itself, it is now believed that cholesterol only becomes a problem once the cholesterol carrier, low-density lipoprotein (LDL), becomes oxidized (attacked by free radicals). The PON1 enzyme attaches itself to high-density lipoprotein (HDL), which protects both HDL and LDL from oxidation. ^{xxxii} Due to common SNPs in the PON1 gene, blood levels of PON1 can vary by a factor of 10 to 40-fold among different individuals. ^{xxxiii,xxxiv} Those with low levels of PON1 have higher levels of oxidized LDL, which can lead to diminished cardiovascular health. ^{xxxv,xxxvi}	MAXIMUM SUPPORT + +
SNP: CYP11B2 (Aldosterone Synthase)	Maintaining blood pressure within the normal range is essential to a healthy heart. The CYP11B2 gene encodes an enzyme called aldosterone synthase, which plays a role in regulating blood pressure. A SNP on the CYP11B2 gene can decrease the ability of blood vessels to relax and constrict in response to changing demands for blood flow. ^{xxxvii} (For example, extra blood flow is needed during exercise.) That inability of the vessels to respond properly can set the stage for cardiovascular issues down the road. ^{xxxviii}	Optimum Genetic Function - -
SNP: ApoB (Apolipoprotein B)	Cholesterol is carried through the bloodstream on various lipoproteins: low-density lipoprotein (LDL), high-density lipoprotein (HDL), and very low-density lipoprotein (VLDL). Apolipoproteins make up the protein part of lipoproteins. One of the more researched apolipoproteins is apolipoprotein B (ApoB); it constitutes the protein component of LDL, the "bad" kind of cholesterol carrier. In fact, without ApoB, LDL cannot form. Because people with SNPs on the ApoB gene have higher ApoB levels, they experience moderate increases in total cholesterol, LDL cholesterol, and triglycerides, ^{xxxix,xl,xli,xlii} as well as impaired glucose tolerance ^{xliii} and increased blood lipid response after meals. ^{xliiv}	ADDED SUPPORT + -

Interpreting your Healthy Aging DNA Assessment results support level.

No disadvantage gene SNPs in this nutritional health area

A **GREEN** test result (Homozygous Negative) predicts that you do not have the variant SNP and that the gene is functioning optimally to produce its specific enzyme, hormone, cytokine or structural protein. A comprehensive **BASIC** nutritional support for this area is added to keep the body functioning optimally.

Optimum Genetic Function	Homozygous Negative Neither chromosome carries the SNP
- -	

One disadvantaged gene SNP from one of your parents in this nutritional health area

An **YELLOW** test result (Heterozygous Positive) indicates that you have one variant SNP and that the protein molecule expressing a specific enzyme, hormone, cytokin or structural protein is functioning less than optimal. As a result, it is important to have **ADDED** nutritional support (SNPNutrients™) for this area to keep body functioning optimally.

ADDED SUPPORT	Heterozygous Positive One chromosome carries the SNP
+ -	

Two disadvantaged gene SNPs from both of your parents in this nutritional health area

A **RED** test result (Homozygous Positive) indicates that you have two variant SNPs and that protein molecule expressing a specific enzyme, hormone, cytokine or structural protein is functioning minimally. As a result, it is important to have **MAXIMUM** nutritional support (SNPNutrients™) for this area to keep the body functioning optimally.

MAXIMUM SUPPORT	Homozygous Positive Two chromosomes carry the SNP
+ +	

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These statements have not been evaluated by the Food and Drug Administration.

Profiling technologies by Genelink BioSciences, Inc. U.S. Patent No. 6,291,171. Additional patents pending worldwide.



REFERENCES

- ⁱ Morrison NA et al. Prediction of bone density from vitamin D receptor alleles. *Nature*. 1994;367(6460):284-7.
- ⁱⁱ Thakkinstan A et al. Haplotype analysis of VDR gene polymorphisms: a meta-analysis. *Osteoporos Int*. 2004;15(9):729-34.
- ⁱⁱⁱ Thakkinstan A et al. Meta-analysis of molecular association studies: vitamin D receptor gene polymorphisms and BMD as a case study. *J Bone Miner Res*. 2004;19(3):419-28.
- ^{iv} Valdivielso JM, Fernandez E. Vitamin D receptor polymorphisms and diseases. *Clin Chim Acta*. 2006 Sep;371(1-2):1-12.
- ^v D'Alesio A et al. Two single-nucleotide polymorphisms in the human vitamin D receptor promoter change protein-DNA complex formation and are associated with height and vitamin D status in adolescent girls. *Hum Mol Genet*. 2005;14(22):3539-48.
- ^{vi} Marco MP et al. Influence of vitamin D receptor gene polymorphisms on mortality risk in hemodialysis patients. *Am J Kidney Dis*. 2001;38(5):965-74.
- ^{vii} Dawson-Hughes B et al. Effect of calcium and vitamin D supplementation on bone density in men and women 65 years of age or older. *N Engl J Med*. 1997;337(10):670-6.
- ^{viii} Morisseau C and BD Hammock. Epoxide hydrolases: mechanisms, inhibitor designs, and biological roles. *Annu Rev Pharmacol Toxicol*. 2005;45:311-33
- ^{ix} Hosoe K et al. Study on safety and bioavailability of ubiquinol (Kaneka QH) after single and 4-week multiple oral administration to healthy volunteers. *Regul Toxicol Pharmacol*. 2007;47(1):19-28.
- ^x Ross D et al. NAD(P)H:quinone oxidoreductase 1 (NQO1): chemoprotection, bioactivation, gene regulation and genetic polymorphisms. *Chem Biol Interact*. 2000 Dec 1;129(1-2):77-97.
- ^{xi} Robinson BH. The role of manganese superoxide dismutase in health and disease. *J Inherit Metab Dis* 1998;21:598-603.
- ^{xii} Bandy B and AJ Davison. Mitochondrial mutations may increase oxidative stress: implications for carcinogenesis and aging? *Free Radic Biol Med* 1990;8:523-39.
- ^{xiii} Rayman MP. Selenium in cancer prevention: a review of the evidence and mechanism of action. *Proc Nutr Soc* 2005 Nov;64(4):527-42.
- ^{xiv} Hu YJ and AM Diamond. Role of glutathione peroxidase 1 in breast cancer: loss of heterozygosity and allelic differences in the response to selenium. *Cancer Res* 2003;63(12):3347-51.
- ^{xv} Hu Y et al. Allelic loss of the gene for the GPX1 selenium-containing protein is a common event in cancer. *J Nutr* 2005;135(12 Suppl):3021S-3024S.
- ^{xvi} Ratnasinghe D et al. Glutathione peroxidase codon 198 polymorphism variant increases lung cancer risk. *Cancer Res* 2000 Nov 15;60(22):6381-3.
- ^{xvii} Moscow J. A., Schmidt L., Ingram D. T., Gnarr J., Johnson B., Cowan K. H. Loss of heterozygosity of the human cytosolic glutathione peroxidase I gene in lung cancer. *Carcinogenesis* (Lond.), 15: 2769-2773, 1994.
- ^{xviii} Cunnane G et al. Early joint erosions and serum levels of matrix metalloproteinase 1, matrix metalloproteinase 3, and tissue inhibitor of metalloproteinases 1 in rheumatoid arthritis. *Arthritis Rheum* 2001;44:2263-2274.
- ^{xix} Dörr S et al. Association of a specific haplotype across the genes MMP1 and MMP3 with radiographic joint destruction in rheumatoid arthritis. *Arthritis Res Ther* 2004;6(3):R199-207.
- ^{xx} Refsum H et al. Homocysteine and Cardiovascular Disease. *Ann Rev Med* 1998;49:31-62.
- ^{xxi} Eikelboom J et al. Homocyst(e)ine and Cardiovascular Disease: A Critical Review of the Epidemiological Evidence. *Ann Intern Med* 1999;131:363-375.
- ^{xxii} Hankey G et al. Homocysteine and Vascular Disease. *Lancet* 1999;354 (9176): 407-413.
- ^{xxiii} Gaughan DJ et al. The methionine synthase reductase (MTRR) A66G polymorphism is a novel genetic determinant of plasma homocysteine concentrations. *Atherosclerosis*. 2001;157(2):451-6.
- ^{xxiv} Guéant-Rodriguez RM et al. Association of MTRRA66G polymorphism (but not of MTHFR C677T and A1298C, MTRA2756G, TCN C776G) with homocysteine and coronary artery disease in the French population. *Thromb Haemost*. 2005;94(3):510-5.
- ^{xxv} Barbosa PR et al. Association between decreased vitamin levels and MTHFR, MTR and MTRR gene polymorphisms as determinants for elevated total homocysteine concentrations in pregnant women. *Eur J Clin Nutr*. 2007, *in press*.
- ^{xxvi} Frosst P et al. A candidate genetic risk factor for vascular disease: a common mutation in methylenetetrahydrofolate reductase. *Nat Genet* 1995; 10:111-113.
- ^{xxvii} Jacques PF et al. Relation between folate status, a common mutation in methylenetetrahydrofolate reductase, and plasma homocysteine concentrations. *Circulation* 1996;93: 7-9.
- ^{xxviii} Lee et al. Tumor necrosis factor-alpha promoter -308 A/G polymorphism and rheumatoid arthritis susceptibility: a metaanalysis. *J Rheumatol*. 2007;34(1):43-9.
- ^{xxix} Alvarez V et al. Association between the TNFalpha-308 A/G polymorphism and the onset-age of Alzheimer disease. *Am J Med Genet*. 2002;114(5):574-7.
- ^{xxx} Witte JS et al. Relation between tumour necrosis factor polymorphism TNFalpha-308 and risk of asthma. *Eur J Hum Genet*. 2002;10(1):82-5.

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- ^{xxxix} Elahi MM et al. A variant of position -308 of the Tumour necrosis factor alpha gene promoter and the risk of coronary heart disease. *Heart Lung Circ.* 2007 Jun 18; [Epub ahead of print]
- ^{xxxvii} Aviram M et al. Paraoxonase inhibits high-density lipoprotein oxidation and preserves its functions: a possible peroxidative role for paraoxonase. *J Clin Invest.* 1998;101:1581-1590.
- ^{xxxviii} Garin et al. Paraoxonase polymorphism Met-Leu54 is associated with modified serum concentrations of the enzyme. A possible link between the paraoxonase gene and increased risk of cardiovascular disease in diabetes. *J Clin Invest.* 1997;99(1):62-6.
- ^{xxxix} Humbert R et al. The molecular basis of the human serum paraoxonase activity polymorphism. *Nat Genet.* 1993;3:73-76.
- ^{xl} Robertson KS et al. Human paraoxonase gene cluster polymorphisms as predictors of coronary heart disease risk in the prospective Northwick Park Heart Study II. *Biochim Biophys Acta* 2003;1639(3):203-12.
- ^{xli} Voetsch B et al. The Combined Effect of Paraoxonase Promoter and Coding Region Polymorphisms on the Risk of Arterial Ischemic Stroke Among Young Adults. *Arch Neurol.* 2004;61(3):351-356.
- ^{xlii} Ylitalo et al. Baroreflex sensitivity and variants of the renin-angiotensin system genes. *J Am Coll Cardiol.* 2000;35(1):194-200.
- ^{xliiii} Hautanen A et al. Joint Effects of an Aldosterone Synthase (CYP11B2) Gene Polymorphism and Classic Risk Factors on Risk of Myocardial Infarction. *Circulation* 1999;100:2213.
- ^{xliiiii} Benn M et al. Polymorphism in APOB Associated with Increased Low-Density Lipoprotein Levels in Both Genders in the General Population. *J Clin Endocrinol Metab* 2005;90(10):5797-5803.
- ^{xl} Talmud PJ et al. Apolipoprotein B gene variants are involved in the determination of serum cholesterol levels: a study in normo- and hyperlipidaemic individuals. *Atherosclerosis* 1987;67:81-89.
- ^{xli} Law A et al. Common DNA polymorphism within coding sequence of apolipoprotein B gene associated with altered lipid levels. *Lancet* 1986;1:1301-1303.
- ^{xlii} Hegele RA et al. Apolipoprotein B-gene DNA polymorphisms associated with myocardial infarction. *N Engl J Med* 1986;315:1509-1515.
- ^{xliiii} Bentzen J et al. Further studies of the influence of apolipoprotein B alleles on glucose and lipid metabolism. *Hum Biol* 2003;75(5):687-703.
- ^{xliiii} Moreno-Luna R et al. Two independent apolipoprotein A5 haplotypes modulate postprandial lipoprotein metabolism in a healthy Caucasian population. *J Clin Endocrinol Metab* 2007;92(6):2280-5.

SAMPLE

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