

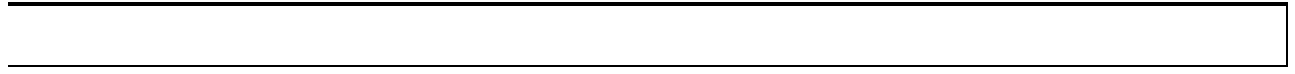


# Your Genetic Compass™

*How genomic sciences have ushered in the  
new era of personalized nutrition*

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# Your Genetic Compass<sup>©</sup>

HOW GENOMIC SCIENCES HAVE USHERED IN  
THE NEW ERA OF PERSONALIZED NUTRITION

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Millions of Americans are taking food supplements in a never ending battle to stay young, feel better, and treat their ills. They take these based on what they read, see and hear with a small percentage actually getting advice from their healthcare practitioners. For most, this guessing game leaves people uncertain, confused and often ingesting supplements that are not specific to their individual needs.

How is one to choose from the hundreds of nutritional supplements?

With over half of the population of the United States taking nutritional supplements the vast majority are uncertain as to what they're taking and why. Many times this shot-gun approach leads to the over (or under) consumption of vitamins and minerals. For the most part, the very nutrients the body craves never make it into the shopping cart.

In the last sixty years, the nutritional science has pushed forward and made tremendous breakthroughs in this area. The era of 'one size fits all' is coming to an end.

In a book published in the 1950's entitled *Biochemical Individuality*, University of Texas biochemist, Roger Williams argued:

*"Each of us has a unique chemical makeup that induces various responses to foods, drugs and the environment. The reason we are unique is that our genes are different."*

This unique chemical makeup has sparked the interest of several areas of health and have created the fields of Pharmacogenetics and Nutrigenetics. Pharmacogenetics is the prospect of combining pharmacology and genomic capabilities. This science would be a breakthrough because more than 100,000 people die each year as a result of adverse responses to medications that are beneficial to thousands of other individuals. 2.2 million people experience serious reactions and others don't respond at all. In combination with genetics each individual's genetic makeup can be assessed before prescribing a generic product. Nutrigenetics would also examine the individual's unique make-up and determine which vitamins, minerals, and other nutrients are necessary for optimal health.

We have mapped our genetic structure and we are unraveling the working of human biology. This has enormous implications including a new understanding of what specific nutrients best serve our unique genetic, physical and bio-chemical makeup. Nutrients along with certain lifestyle modifications, can support our strengths and balance our weaknesses.

Our genes hold the answer to determining our lifestyle and nutrient well being.

## GENOMICS AS A TOOL FOR WELLNESS

Genomics, as a segment of the healthcare industry, can potentially illuminate the path to avoiding serious illness. With rising health care costs and the cost of pharmaceutical medications soaring, more people are taking health into their own hands. Not only are they seeking alternative therapies for their ailments, but they are thinking more about prevention. However, the messages about how to stay healthy have been overwhelming and quite mixed. There is no clear-cut answer as to how to stay healthy.

We now have the opportunity to catch a glimpse of our unique risk of developing certain conditions through DNA testing. Not only will we be able to determine which areas of our own health we should focus on, but some direction as to which nutritional products will best serve our individual needs in the area of preventive health.

Best-selling author, economist and futurist Paul Zane Pilzer, in his book *The Next Trillion* wrote:

*"By examining a person's DNA, which can be taken from the mouth with just a small swab or scraping device. It is already possible to predict the probability that a person will develop certain diseases. And soon, based on the recently completed mapping of the human genome, it should be possible to predict every forthcoming disease or condition not caused by external (i.e. diet and exercise) factors.*

Genomic Science has given physicians one more tool to use when treating their patients. A physician may use DNA testing to find out his patient's starting point for health, then with further testing the physician can determine where his patient has been. It is at this point that a physician will best be able to work with his patient to establish the most appropriate program available for that individual, including nutritional supplements.

## GENOMICS - THE HUMAN BOOK OF LIFE

Genome science began formally in 1990 with the establishment of the Human Genome Project. This enormous project is the combined effort between the United States Department of Energy and the National Institutes of Health. The project was based on the mission of pursuing a greater understanding of individual health risks. The Human Genome Project goals were to generate a high-quality reference sequence and identify all human genes, as well as enhance computational resources to support future research and commercial applications.

There are approximately 35,000 genes in the Human Genome, however, functions for more than half of discovered genes are unknown. Genes are made up of DNA base pairs arranged in a double-helix formation. Our individual uniqueness lies in the small differences of bases that can exist where single base DNA differences (SNPs) occur in humans. The SNP information promises to revolutionize the process of finding gene locations for disease-associated sequences. Finding the DNA sequences underlying such common diseases as cardiovascular disease, diabetes, arthritis, and cancer is being aided by the human SNP

maps. These genes and SNPs provide focused targets for the development of effective new therapies.

### ***Our physical uniqueness is largely due to SNPs***

The DNA between any two humans is about 99.9% identical. Except for identical twins, variations in just a small fraction of our DNA account for the major ways in which one human is different from another. These small variations in DNA are called SNPs, which stands for 'single nucleotide polymorphisms' or (SNPs, pronounced 'snips'). Scientists have identified about 1.4 million locations where single-base DNA differences occur in humans. This information promises to revolutionize the process of finding chromosomal locations for disease-associated sequences.

Researcher Bruce Ames Ph.D., from the Department of Cell and Molecular Biology at University of California, Berkeley wrote in his review article in the Proceedings of the National Academy of the Sciences: *Cancer Prevention and Diet: Help from Single Nucleotide Polymorphism:*

*"...Understanding causality is the prerequisite for effective action. Causality can be established by combining epidemiology, a key tool for identifying major risk factors, with research on mechanism. It is becoming apparent that a better understanding of nutrition and nutrition-genetic interaction will be one important consequence of the genomic revolution."*

### ***How the knowledge of SNPs can be used to improve our lives***

The awesome feat of compiling the Book of Life was accomplished by technologies that spelled out the entire human DNA genome (made up of the chemical base pairs symbolized by the letters A,G,C and T). Simply, we can think of DNA as a string of 3 billion of these letters, in which the sequence of letters follows a precise order. If we compare the DNA sequence of any two people, we sometimes see variation in a letter. This letter variation is a SNP. For example, at a specific position along the string of DNA, one person may have the letter "A " whereas another person may have the letter "T". These variations (SNPs) occur, on average, once in every 2,000 letters of the DNA.

- Pharmacogenetics: SNPs seem to explain why people react differently to different types or amounts of medicines. For example, patients can react differently to the same heart medication, such as a "beta-blocker". Since SNPs can affect the structure and function of proteins and enzymes, they can influence how efficiently a medicine is absorbed and metabolized. A major goal of the pharmacogenetics industry is to use the science of SNPs to determine which drugs are most suitable for any given patient.

## THE NEW SCIENCE OF NUTRAGENETICS

**N**utrigenetics is a combination of the sciences of genetics and nutrition that reveals personalized information regarding an individual's status and provides the basis for selecting a dietary and nutritional program best suited to achieving the healthiest and longest life possible.

- Nutrigenetics uses SNP testing to identify areas of an individual's genetic make-up that may be functioning less than optimally.
- Nutrigenetics will help guide individuals in choosing the optimal combination of nutrients and vitamins, matched to their unique genetic make-up.

For the first time, this revolutionary SNP science is making it possible to personalize and tailor health care products. How is this done?

### ***SNPs guide personalization of nutrient formulations.***

The SNP profile test examines a variety of genes which are responsible for making proteins that play key biochemical roles. These include oxidative stress, heart and circulatory health, immune health, bone health, and defense against environmental pollutants.

#### **Key Point**

If the SNP test predicts that you might not be as efficient as possible in any given health area, you can do something about it. For every SNP tested, there are compensating enhancing nutrients that can put you on the path toward optimal health. Thereby complementing your body and eliminating the guesswork of formulating a nutritional supplement program.

It is logical then that everyone should use a basic multivitamin and mineral formulation to cover the major areas of nutrition, and only take additional ingredients based upon the SNP test.

#### **Key Point**

This means that now you can use a more scientific approach to being proactive in doing your best to prevent health problems that might otherwise occur later in life. We all know that good nutritional care is important in preventing cancer, heart disease and osteoporosis, and in defending against other diseases.

Again, Researcher Bruce Ames Ph.D., in *Cancer Prevention and Diet: Help from Single Nucleotide Polymorphisms*, wrote:

*"Optimizing micronutrient intake (through better diets, fortification of foods, or multivitamin-mineral pills) can have a major impact on public health at low cost. Other micronutrients are likely to be added to the list of those whose deficiency causes DNA damage in the coming years. Tuning-up human metabolism, which varies with genetic constitution and changes with age, is likely to be a major way to minimize DNA damage, improve health, and*

*prolong healthy lifespan, and a drop of blood [a cheek swab] or a gene chip could be part of the way to accomplish this."*

Further:

*"It is already apparent that there are many polymorphisms that influence risk in heart disease. Single nucleotide polymorphisms provide a powerful molecular tool for investigating the role of nutrition in human health and disease, and their integration into clinical, metabolic, and epidemiologic studies can contribute enormously to the definition of optimal diets.*

### **The impact of Genetic Science reaches into disease prevention.**

The information in the Book of Life is revolutionizing clinical medicine as well as preventive health programs including Nutrigenetics. SNPs not only account for many of our physical differences, but they also account for our biochemical differences. Being 'more or less' efficient in one biochemical pathway, may have long term consequences related to how well we can fight disease, or even how rapidly we age.

Through Nutrigenetics, people are able to influence their own health outcomes.

## **APPLICATIONS OF SNP TESTING: OXIDATION - THE PARADOX OF LIFE**

**W**e are exposed every moment of our lives to highly reactive and toxic molecules, called reactive oxygen species (ROS) that damage our bodies. From the moment we are conceived to the day we die, oxidation of critical proteins, lipids, nucleic acids and sugars occurs in every cell in our bodies. One strongly supported theory of aging (and of many age-related diseases) is that uncorrected oxidative events result in the deterioration of cellular function.

### **Key Point**

Over time the accumulation of oxidative events harm's cell machinery and DNA as well as damaging critical proteins and lipids. This creates sub-optimal function of organs, which leads to aging in general as well as to specific vulnerability to age-related diseases.

There are several sources of ROS. One such source of ROS occurs while burning sugar to generate energy. Indeed, it is estimated that 3 to 5% of all sugar that we consume is converted to ROS in our bodies. In other words, to live – we must burn – and this burning of sugar causes damage. Our immune system produces many ROS in the process of fighting and destroying pathogens. Free radicals are a normal part of our inner environment.

Lifestyle also affects our exposure to environmental agents that cause production of ROS. For example, cigarette smoke contains many substances that dramatically increase ROS and exposure to sunlight increases oxidation of the skin. On a daily basis we are inadvertently exposed to many environmental substances which increase oxidation in the body.

The body's defenses against oxidation and ROS include several important enzymes and proteins that increase the rate of beneficial chemical reactions. The major function of these anti-oxidant enzymes is to convert ROS to non-toxic substances. One such enzyme, superoxide dismutase (SOD), when made in a less than optimal form has been linked to increased risk for macular degeneration, a condition in which the eye breaks down. In this case, the inability of 'less than optimal SOD' to completely neutralize ROS in the eye exposes our eyes over time to greater damage. Other anti-oxidant enzymes as well as anti-oxidant vitamins and minerals are also associated with effective removal of ROS. Therefore, with a 'less than optimal SOD', it is possible to compensate with other anti-oxidants supplied through the diet. The effective functioning of an antioxidant defense system is critical to countering the aging process and for the prevention of related degenerative conditions. Indeed, in animal models, enhanced activity of many of these anti-oxidant enzymes is associated with increase life span.

The only source of other important anti-oxidant compounds is from our diet or from supplementation. Vitamins are molecules that the body cannot synthesize. Many of these vitamins are anti-oxidants that play a critical role in the protection of the body from ROS. As essential vitamins, there is a need for a daily ingestion of these anti-oxidants to maintain life and to protect the body from the effects of ROS. Therefore a minimal daily intake is required for anti-oxidants to help counter the never-ending production of ROS.

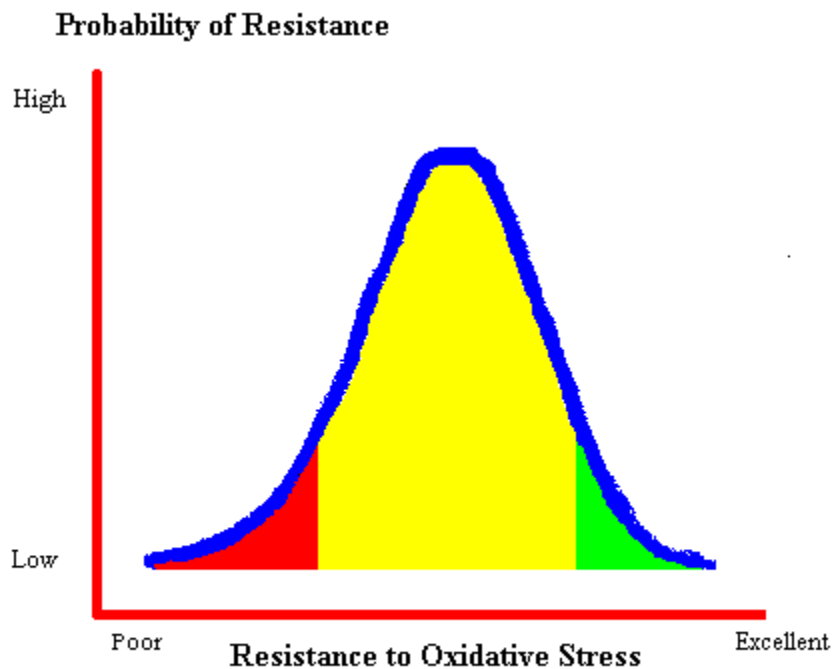
**Key Point**

Can we slow the aging process by increasing the intake of anti-oxidant vitamins? Yes. There are now numerous published reports showing that in animal models, supplementation of the diet with anti-oxidants, at levels higher (and usually many fold higher) than the recommended minimum daily intake of anti-oxidants, can slow aging of memory and motor function and increase the life span.

## PROBABILITY OF RESISTANCE TO OXIDATIVE STRESS

There appears to be a small subset of the human population who handle the ravages of oxidative stress better than most of us. For these fortunate individuals, both parents provided them with a battery of optimal genetic response pathways to deal with oxidative stress. These individuals would best be defined, perhaps, as the upper 5% of a probability bell curve of the entire population's measured ability to handle oxidative stress, Figure 1.

Figure 1. The probability bell curve of humankind's ability to handle oxidative stress.



Likewise, there is another 5% at the lower end of the curve who, for reasons of the genetic lottery, received little protective abilities from either parent. These individuals handle oxidative stress minimally.

Then there are the rest of us - everyone else who fits somewhere inside the 90% portion of the bell curve in our abilities to handle oxidative stress. Some of us are higher on the curve, some lower, but regardless of where we fall on the curve, we all require some additional help.

## CUSTOMIZING PERSONAL CARE FORMULATIONS BASED ON NEEDS

### *Building Better Nutritional Supplement Programs Based on Bioindividuality*

**A**long with blood tests, urinalysis and hair analysis, a genetic profiling from a simple cheek swab can be a very useful tool. In combination with a patient's lifestyle and metabolic factors, genetic tests give physicians more insight into treating their patients as individuals. A person's genetic profile is part of what makes us unique and can produce different nutritional needs based upon Biochemical Individuality. From the results of genetic evaluation and SNP analysis combined with an understanding of metabolic pathways and biochemistry, it is possible to make recommendations for specific nutritional products for that person. As one puts together information gained from metabolic, genetic and lifestyle evaluation, even better customized nutritional formulations can be designed to fit the needs of the individual.

## INFORMATION ON PATIENT RESULTS

**A**s the preceding sections have described, the science of applied genetics is developing rapidly and has now progressed into realms that are practical for long-term health maintenance considerations. Accordingly, the GeneLink scientific and medical advisory board has selected a group of genes that are important to oxidative stress that affect metabolic health. While not absolutely linked to the onset of specific degenerative diseases these genes are directly linked to important metabolic pathways that affect an individual's health.

### **Key Point**

The specific SNPs chosen are related to the relative biochemical activities (efficiency) of the genes and their product proteins that occur at relatively high frequencies in the population. All of these genes are well characterized in the scientific literature. Furthermore, they are linked to metabolic pathways where specific compensatory supplementation can be defined.

Thus, the GeneLink SNP profiles in Nutrigenetics allow you to offer your patients a personalized approach to nutritional supplement selection that targets individual requirements. A sample profile report is shown in Figure 2:

Figure 2. – Sample Nutrigenetic Profile Panel for General Nutritional Assessment

Column 1 Functional Area	Column 2 PHYSIOLOGIC SYSTEM							Column 3 Recommended Support
	Aging	Cardiovascular	Detoxification	Immune	Neurologic	Pulmonary	Skeletal	
Oxidative Stress -1	✓	✓	✓	✓	✓	✓	✓	
Oxidative Stress -2	✓	✓	✓	✓	✓	✓	✓	
Detoxification	✓		✓			✓		
Heart, Circulatory Health -1	✓	✓	✓					
Heart, Circulatory Health -2	✓	✓			✓			
Immune Health	✓	✓		✓				
Bone Health	✓	✓					✓	

As described in the preceding sections, the testing is done by noninvasive cheek swab collection of a sample which is then sent via a confidentially coded process to our laboratory with the patented GeneLink kit. The example report (Figure 2) shows how the SNP testing results are represented to you and your patient.

First, the Functional Health Area (Column 1), associated with the specific SNP that is listed. The results for each SNP show a color-coded indicator (Column 3) of whether the individual requires Basic Support, Added support, or Extra Added support. In addition, there is an informational “check-box index” (Column 2) that shows the physiologic system’s that are most affected by the metabolic pathway tested. Because this is not a medical “diagnostic” test, the SNP testing results are currently reported as informational only. Yet, as noted, these results are based on extensive scientific literature and have been thoroughly qualified for physiologic relevance prior to their inclusion in the panel. The results are provided to you and your patient as a “genetic compass” for selection of the appropriately matched nutritional supplement.

### What Do the SNP Tests Mean?

GeneLink’s profile method measures the natural variations (SNPs) in human genes. Such variations may result in the production of proteins that function less than optimally. The SNP profile information can be used by others, such as formulators and health care professionals, to provide customized nutrients that are tailored to the needs of an individual.

A green test result (Homozygous Negative) predicts that you do not have any SNPs and that the protein molecules expressed by this given gene, are functioning optimally to produce its specific enzyme, hormone, cytokine or structural protein. A comprehensive nutritional foundation product is recommended to keep this system functioning optimally.

A yellow test result (Heterozygous Positive) indicates that you have one variant SNP and one non-variant SNP and that a portion of the protein molecules expressed by this given gene, are functioning sub-optimally to produce a specific enzyme, hormone, cytokine or structural protein. In order to compensate for the less than optimal function of the protein molecule, additional nutritional support is recommended.

A red test result (Homozygous Positive) indicates that you have two variant SNPs and that the protein molecule expressing a specific enzyme, hormone, cytokine or structural protein is functioning minimally. As a result, it is important to have a strategic nutritional supplementation program in place to compensate for this inferior protein molecule.

### **Oxidative Stress-1 Gene (OS-1 gene), Manganese Superoxide Dismutase-1 (MnSOD)**

- **General Description** - The OS-1 gene plays a major role in protecting the body against oxidative stress. Oxidative stress is caused by free radical molecules that can damage DNA, protein and lipid. In this way, oxidative stress can affect virtually every cell and, hence, every area of health. During the process of respiration, the oxygen that becomes consumed by every cell also ends up generating oxygen radicals as natural by-products. The cells use the OS-1 enzyme to prevent the build-up of excess oxide radicals that otherwise may damage the cell machinery and its DNA.
- **Specific Information About the Enzyme** - MnSOD (Manganese Superoxide Dismutase) is the key enzyme that detoxifies superoxide radicals by the dismutase reaction. The superoxide radicals are generated in the mitochondria and are produced from electrons that leak along the electron transport pathway onto atomic oxygen to form oxygen with a single unpaired electron. As much as 2% of oxygen consumed during mitochondria oxidative respiration is converted into superoxide radicals. In this context, MnSOD serves as the first line of defense against a build up of damaging free radicals.
- **Frequency\*** - In general North American populations, approximately 20% are Homozygous Negative (Green), 52% are Heterozygous Positive (Yellow) and 28% are Homozygous Positive, (Red) for this gene SNP area.
- **Complementary Nutritional Supplement** - It is possible to support the body against oxidative stress with certain nutrients called antioxidants. Although unable to increase the body's production of MnSOD, these nutrients also aid the body in the detoxification of superoxide radicals. Specific antioxidant nutrients have extraordinary abilities to combat oxidative stress, such as Vitamins A, C, E and Selenium, as well as Coenzyme Q10, and Alpha Lipoic Acid.

### **Oxidative Stress-2 Gene (OS-2 gene), Glutathione Peroxidase (GPX1)**

- **General Description** - The OS-2 gene also plays a major role in protecting the body against oxidative stress. Its important role is to detoxify hydrogen peroxide, one of the molecules formed during oxidative stress. In so doing, damage to protein, DNA and lipids is avoided.

- **Specific Information About the Enzyme** - Hydrogen peroxide is a product of OS-1. If it is not detoxified, it will decompose into hydroxyl radicals (via iron catalysis). It is important to prevent accumulation of hydroxyl radicals since they are very toxic in being able to abstract electrons from other molecules which in turn form reactive radicals. Preventing the formation of hydroxyl radicals is so important, that the cell employs other enzymes that also detoxify hydroxyl radicals. One such enzyme is GPX (Glutathione Peroxidase) which will reduce hydrogen peroxide to a harmless product which is then excreted.
- **Frequency\*** – In general North American populations, approximately 35% are Homozygous Negative (Green), 48% are Heterozygous Positive (Yellow) and 17% are Homozygous Positive, (Red) for this gene SNP area.
- **Complementary Nutritional Supplement** – It is important to eliminate the harmful effects of hydrogen peroxide from the body and with certain nutrients its detoxification can be supported. Since hydrogen peroxide can be a source of unwanted free radicals which can do further damage to the body, especially to the liver, enhanced antioxidant protection is especially important. Glutathione is the key antioxidant in the liver. The combination of stabilized whey protein and DMG supports the intracellular production of glutathione and protects the liver from reactive oxygen species.

\*Gene frequencies are given for a North American population pool without ethnic sub classification.

## **Detoxification, (Detox)**

### **Human Microsomal Epoxide Hydrolase (mEPHX)**

- **General Description** - The Detox-1 gene plays an important step in the elimination of environmental pollutants such as the widely spread polycyclic aromatic hydrocarbons (PAHs), which are carcinogens found, for example, in cigarette smoke and as products of automobile combustion.
- **Specific Information About the Enzyme** – Environmental pollutants, such as epoxides, can hasten the aging process and infirmity, increase the likelihood of disease and can even initiate cancer. MEPX (microsomal Epoxide Hydrolase) is one enzyme that can metabolize many of the toxic chemical epoxide intermediates.
- **Frequency\*** – In general North American populations, approximately 42% are Homozygous Negative (Green), 48% are Heterozygous Positive (Yellow) and 10% are Homozygous Positive, (Red) for this gene SNP area.
- **Complementary Nutritional Supplement** – Certain nutrients can be utilized to aid the body in the detoxification of and elimination of environmental pollutants. Certain species of blue-green algae can assist the body in the breakdown of metallic toxins and environmental chemicals. As forms of soluble fiber, Beta Glucan and Fructooligosaccharides can aid in the elimination of pollutants as well as activate certain aspects of the immune system.

## **Heart Circulatory Health-1 (HCH-1) Paraoxonase-1 (PON-1)**

- **General Description** - The HCH-1 gene helps to prevent the build-up of plaque on blood vessel walls and, thereby, participates in maintaining blood vessel integrity. Good blood vessel health is an important factor in the avoidance of coronary heart disease.
- **Specific Information About the Enzyme** - When low density lipoproteins (LDLs) become oxidized (e.g., by oxygen radicals generated from oxidative stress), the peroxidized LDLs are scavenged by macrophages which become transformed into foam cells filled with cholesterol esters. These eventually become incorporated into fatty streaks in the endothelium that, in time, can become atheromatous plaques. PON-1 (paraoxonase), which associates with HDL, is able to hydrolyze lipid peroxides before they are consumed by macrophages. In this way, PON-1 has a protective effect against atherosclerosis by preventing the accumulation of peroxidized LDLs.
- **Frequency\*** - In general North American populations, approximately 51% are Homozygous Negative (Green), 42% are Heterozygous Positive (Yellow) and 7% are Homozygous Positive, (Red) for this gene SNP area.
- **Complementary Nutritional Supplement** - If one of the body's natural defenses against abnormal cholesterol levels is compromised, it would be important to have a compensatory defense. Some very effective nutrients in supporting cholesterol levels within normal ranges include Red Rice Yeast, Picosanols, Phytosterols, EPA and Chromium Picolinate.

\*Gene frequencies are given for a North American population pool without ethnic sub classification.

## **Heart, Circulatory Health-2 (HCH-2) Methylenetetrahydrofolate Reductase (MTHFR)**

- **General Description** - The HCH-2 gene helps to prevent the build up of homocysteine in the blood. Elevated homocysteine causes oxidation of LDLs, increases the risk of venous thrombosis, and damage to the blood vessels.
- **Specific Information About the Enzyme** - MTHFR (Methylenetetrahydrofolate Reductase) is an important enzyme in the folic acid pathway. MTHFR is responsible for catalyzing the transformation of homocysteine to methionine. As a consequence, a build up of homocysteine is prevented by the action of MTHFR.
- **Frequency\*** - In general North American populations, approximately 43% are Homozygous Negative (Green), 43% are Heterozygous Positive (Yellow) and 14% are Homozygous Positive, (Red) for this gene SNP area.
- **Complementary Nutritional Supplement** - It is necessary to support the reduction of homocysteine build-up in the blood to reduce the risk of cardiovascular problems. There are several pathways that address this reduction and promote the formation of other

products such as methionine or important sulfur-containing proteins. Certain nutrients encourage this transformation, including Vitamins B12, B6, and Folic Acid, Acetyl-L-Carnitine, Magnesium, Potassium, Dimethylglycine, Betaine, and Coenzyme Q10.

### **Immune gene (IM) Tumor Necrosis alpha (TNF-A)**

- **General Description** - The Im-1 gene plays multiple functions in immune responses. It plays a key role in signaling immune cells to areas of physical injury or infection and increasing the numbers of immune cells.
- **Specific Information About the Enzyme** - TNF-Alpha (Tumor Necrosis Factor alpha) is secreted by macrophages and neutrophils and has long-range effects on defending against infection and injury by signaling the recruitment of T and B cells. It is the key activator of NF-kappa-B that is the master regulator of immune response genes. These are just some of the effects of TNF-Alpha that are beneficial to the host in controlling infection. TNF-Alpha is also associated with inflammation, cytotoxicity, antiviral activity and the proliferation of immune cells.
- **Frequency\*** - In general North American populations, approximately 77% are Homozygous Negative (Green), 21% are Heterozygous Positive (Yellow) and 02% are Homozygous Positive, (Red) for this gene SNP area.
- **Complementary Nutritional Supplement** - TNF-Alpha is important in encouraging the proliferation as well as recruiting immune cells to the site of an infection. It is possible to compensate nutritionally for the areas of the immune system which might be affected by a compromised gene expressing TNF-Alpha. Nutrients such as Dimethylglycine, Maitake mushroom, Larch Tree Extract, and Beta Glucan are known to be immune system modulators.

### **Bone Health gene (BH) Type I collagen alpha 1 (COL1A1)**

- **General Description** - The BH-2 gene is responsible for producing a protein that is a major component of bone. Having the correct amount and proportion of the BH-2 protein in the bone is important for good structural bone health.
- **Specific Information About the Enzyme** - The type-1 collagen protein is the most abundant protein of bone, skin and tendons. This is a structural protein made up of two protein chains: alpha 1 and alpha 2. The genes that encode alpha 1 and alpha 2 must be tightly regulated. Overproduction of the alpha 1 chain by the COL1A1 gene has been associated with lower bone mineral density.
- **Frequency\*** - In general North American populations, approximately 75% are Homozygous Negative (Green), 23% are Heterozygous Positive (Yellow) and Homozygous Positive, (Red) for this gene SNP area.
- **Complementary Nutritional Supplement** - Bone mineral density can be supported by many nutritional factors. Such nutrients as Calcium Hydroxyapatite, Magnesium, Boron, Vitamins D, C, B6, B12 and Folic Acid, as well as Chondroitin Sulfates, Ipriflavone,

Resveratrol and Zinc support collagen production and the building of strong and healthy bones.

\*Gene frequencies are given for a North American population pool without ethnic sub classification.

## A SAMPLE NUTRAGENETIC PROFILE AND ACCOMPANYING RECOMMENDATIONS

Figure 2. – Sample Nutrigenetic Profile Panel for General Nutritional Assessment

Functional Area	PHYSIOLOGIC SYSTEM							Recommended Support
	Aging	Cardiovascular	Detoxification	Immune	Neurologic	Pulmonary	Skeletal	
Oxidative Stress -1	✓	✓	✓	✓	✓	✓	✓	Added Support
Oxidative Stress -2	✓	✓	✓	✓	✓	✓	✓	Basic Support
Detoxification	✓		✓			✓		Basic Support
Heart, Circulatory Health -1	✓	✓	✓					Maximum Support
Heart, Circulatory Health -2	✓	✓			✓			Added Support
Immune Health	✓	✓		✓				Maximum Support
Bone Health	✓	✓					✓	Basic Support

The results of the genetic test are clearly identified as can be seen in the example above. But how do we translate the results of the test to the nutritional support that we need? Each product that corresponds to specific functional area are clearly labeled and specific recommendations are listed according to the level of need. Please see the following for a list of nutritional support products that would be recommended for this specific patient.

Functional Area	Level of Support	Recommended Nutritional Supplement	Amount of Support
Oxidative Stress-1	Added Support	OS-1	2 caps, once daily
Oxidative Stress-2	Basic Support	Spectra-SNP	3 tabs, twice daily
Detoxification	Basic Support	Spectra-SNP	————
Heart, Circulatory Health-1	Maximum Support	HCH-1	3 caps daily
Heart, Circulatory Health-2	Added Support	HCH-2	2 tabs, daily
Immune Health	Maximum Support	IM	1 tab, three times daily
Bone Health	Basic Support	BH	————

It can be seen from this example that every functional area that is green, or labeled Basic Support, would receive a recommendation for a foundation product to support optimal health (it is unnecessary to repeat the foundation product for more than one green functional area). The amount of support needed depends upon the level of support reported by the individual genetic test.

## Frequently Asked Questions

### 1. Why should I use a GeneLink's Profile Assessment for personalizing my nutritional program?

Not everyone is alike – and not everyone responds to nutrients, or even medicines in the same way.

In the absence of a sophisticated measurement tool such as GeneLink's Profile Assessment, most people are forced to simply guess which nutritional products are right for them.

GeneLink's powerful Nutrigenetic Profile Assessment™ provides a scientific basis for more accurately predicting your unique needs. This information is used to guide tailored nutritional formulations to help you achieve optimal health and performance.

You can expect superior results, improved health benefits and the peace of mind that comes from knowing you are taking advantage of a scientifically personalized program that is focused on your unique physiologic makeup.

### 2. Why don't I just take handfuls of multi-vitamins to cover everything?

Although it's possible to 'just take handfuls' of multi-vitamins, most health professionals would agree it certainly isn't practical; The average person simply can't afford nor would they be able to easily swallow all of the ingredients required to "cover all their bases." Also, there is increasing evidence that taking *too much* of certain nutrients may even be harmful.

For example, you can get too much antioxidant protection. Damping down your metabolic system by excessive, *unbalanced* antioxidant intake can cause as many problems as not getting enough. Different free radicals require specific antioxidants –and there is no single antioxidant that addresses all types of free radicals.

Some manufacturers and distributors would have us believe that a 'cookie cutter' or 'one-size-fits-all' approach is good enough. Don't believe it.

When your long-term health and performance is at stake, a personalized scientific approach is best.

### 3. How do I take the test and when are the results returned?

Everything you need is included in GeneLink's Patented Collection Kit™. The process takes about 5 minutes and is easy as brushing your teeth. You simply swab the inside of your mouth (the inner cheeks) with the cotton swabs which are included.

Send the collected sample to GeneLink's laboratories in the pre-addressed, postage paid envelope. Your confidential results are typically delivered in 7-10 business days.

#### **4. What is GeneLink's privacy policy? How does the company plan to ensure my confidential information is kept private?**

GeneLink respects the privacy of every individual and has taken numerous precautions to create a process that will allow individuals to maintain the highest level of privacy.

All information provided by the customer is kept on a secure server and all samples are identified by barcode only. Your private information is never shared with a third-party. GeneLink maintains a strict confidentiality policy.

After the evaluation is completed, all DNA sample material is destroyed.

#### **5. What are the details of the SNP analysis process?**

1. After receiving the swabs, GeneLink's lab extracts the DNA. (All samples are bar coded for confidentiality and control).
2. Next, the lab amplifies the region of the DNA containing the SNP (single nucleotide polymorphism) using what is called a PCR (polymerase chain reaction).
3. The SNP is measured by a single nucleotide base extensions method called SNP-IT™ Technology.
4. The results of these SNP measurements are translated by GeneLink's computers and developed in to a confidential report called a Nutrigenetic Profile™.

#### **6. How accurate is this testing technology?**

There are several types of methods to determine DNA polymorphisms (SNPs). GeneLink utilizes the Single Base Chain Extension (SBCE) assay which is the most accurate method available to detect single nucleotide polymorphisms. The SBCE assay identifies the (SNP) directly on the DNA.

The profile accuracy is nearly 100%. The assay is performed robotically, which virtually eliminates human error in sample manipulation. In rare instances, when a particular SNP area of a profile 'does not read', it is repeated. All repeats thus far have been successful.

#### **7. What is the science behind the determination of a need for Basic Support, Added support and Maximum support?**

There are two copies of every gene, one from each parent. The SNP analysis examines each copy. Moreover, for each gene copy, the SNP will exist as either variant A (e.g., desirable) or variant B (e.g., undesirable).

All individuals will end up with SNP reads of: A/A or A/B or B/B. In this case:

If a person has B/B (Maximum Support is suggested) because that person has two undesirable SNPs.

If a person has A/B (which is less desirable - Added Support is suggested) because that person has only one of the desirable SNPs and an undesirable SNP.

If a person has A/A (Basic Support is recommended) the person receives a basic formulation. (GeneLink agrees with the Journal of American Medicine, The Council for Responsible Nutrition and studies demonstrating that everyone benefits from at least a basic nutritional supplementation or skin-care protection)

GeneLink's statistical results demonstrate that virtually everyone tested will require Added Support and/or Maximum Support in at least one or two gene SNP areas.

### **8. Why are the SNPs used in GeneLink's profiles selected over millions of others?**

There are millions of SNPs. However, only certain subsets are associated with increased risk for disease and physiologic health conditions.

GeneLink selects only 'functional SNPs' which indicate poor enzyme function via epidemiological or biochemical studies.

Additionally, GeneLink selects only those SNPs which can be addressed using nutrients or formulations or lifestyle modifications.

These SNPs physically reside in either the coding region (protein portion) of the gene which can alter enzyme function or they reside in the promoter region which affects the level of expression of the gene in question.

### **9. What is the clinical research that ties nutritional supplements to support SNP predispositions?**

All of the enzymes represented in the SNP profile have been well-studied and there is biochemical evidence in almost every instance that correlates why an enzyme affected by the SNP does not function properly. Additionally, there is leading clinical evidence linking SNPs to nutrition.

Thus, for major enzymatic players of oxidative stress, there is a clear fit with the genetics, epidemiology and biochemistry.

For several of the SNPs, there is a direct link between having the SNP and being able to lower oxidative stress or the medical risks associated with oxidative stress by the ingestion of particular antioxidant nutrients.

For example the SNP for methylenetetrahydrofolate reductase (MTHFR or Heart, Circulatory Health-2), produces an enzyme with decreased affinity (Km) for its direct substrate, 5,10 methylene-THF, which can cause a build up of homocysteine, which is deleterious to heart health. Increasing folic acid (upstream substrate) or the product of the enzyme reaction (5 methyl-THF) can ameliorate the build-up of homocysteine.

For some SNPs there is no definitive clinical evidence available to date that directly links the benefit of a nutrient to the SNP. These studies will come in time. Nevertheless, the fact that the biochemical parameters for all of the SNPs are so well known provides a rational nutritional approach to addressing unfavorable physiological conditions, based on scientific knowledge of how the SNP specifically functions.

### **10. Who conducted the research and who endorses GeneLink's research?**

GeneLink's medical and scientific advisors along with independent academic laboratories and medical centers have conducted nearly 100% of the work. GeneLink's medical and scientific advisors hold positions at major research institutions.

The science and technical information behind GeneLink's technology has been favorably reviewed by the scientific staff department of our various clients and collaborative partners.

Studies have been statistically quantified and involve sophisticated molecular biology, biochemistry and genetic analyses.

## The Future

**W**e anticipate rapid advances in knowledge related to SNPs in the genes of many metabolic pathways. Therefore, we have a vigilant process in place to continually identify SNPs that have potential preventative and health maintenance relevance.

With over half of all adult Americans using supplements, the benefits of being able to more precisely target an individual's nutritional needs seem obvious. Imagine a world in which we know exactly which, or how much of a vitamin, mineral, or nutritional regimen we need for optimal health, energy and well being. For clinicians and practitioners who believe their patient's health interests are best served by cutting edge science, keeping a sharp eye on new advances in genetic science seems a self-prescription worth observing.

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## Glossary of Terms

**Amino acids:** All proteins are made up of amino acids, of which there are 20. The amino acids of each protein are joined together in a unique order that is determined by the DNA genetic code.

**Antioxidant:** Any molecule that eliminates the damaging effects of free radicals, including oxygen free radicals, is an antioxidant. Every cell in our body produces natural antioxidant proteins that prevent the build-up of free radicals. In addition, a variety of natural nutrients including certain vitamins can act as antioxidants that help to eliminate free radicals.

**Base:** Bases (or nucleotides) are the building blocks of DNA. There are four different bases: adenine, thymine, cytosine, and guanine or A, T, C, and G. They are sometimes referred to as genetic letters. The human genome is made up of 3 billion bases that appear to follow a random order ( e.g.,.....AGGCTTAT.....etc), but in fact, the order is actually very precise and forms the string of DNA that defines our genes. The bases make up DNA, and DNA makes up genes, and genes make up chromosomes, which altogether forms the human genome.

**Biochemical Individuality:** Our genetic uniqueness creates demands for specific needs of nutrients beyond the average to facilitate optimal function and prevent premature disease.

**Buccal Swab:** A special device similar in appearance to a Q-tip. It is used to collect DNA by rubbing the cheeks inside the mouth. It provides a simple, quick and non-invasive way to collect DNA.

**Cell:** The smallest unit of a living organism. Cells make up our tissues. A cell is enclosed by a membrane and has an inner nucleus that harbors the entire human genome in the form of DNA. Human cells, which number in the trillions, are specialized and make up the various tissues, e.g., nerve cells make up the brain.

**Chromosome:** The genes are distributed on 46 separate DNA strands called chromosomes. For the relationship between DNA, genes and chromosomes, see Base (above).

**Detoxification:** The process by which the body manages to destroy and clear itself of accumulating harmful substances, such as environmental toxins. This is accomplished by a variety of detoxifying enzymes.

**DNA:** The genetic material of all living organisms is made up of the huge molecule called DNA. DNA itself is made up of the four chemical units called A, G, C and T. Three billion A, G, C, and T units follow one another in a unique order to create the specific DNA chain that forms a human being. Sometimes, even if one base is not in the correct order, disease or the risk of disease occurs.

**Enzymes:** Proteins that carry out all of life's functions, such as metabolizing food, producing energy and controlling movement.

**Free radicals:** Molecules that have an extra electron that enables them to react rapidly with and damage important proteins, DNA and lipids. If not neutralized, an excess of free radicals can destroy cell structures and generate DNA mutations. A ROS (reactive oxygen species) is a specific type of free radical (see below).

**Functional Health Area:** Major organ systems of the body, including heart and circulatory system, nervous system, bone etc.

**Homocysteine:** An amino acid which is normally found in the blood. Increased levels of homocysteine are associated with an increased risk of cardiovascular disease.

**Gene:** A fundamental unit of heredity. The gene contains instructions for making a new protein. Humans may have as many as 100,000 genes. See Base (above) for relationship between DNA, gene, chromosome and genome.

**Gene variation:** A naturally occurring variation in the DNA sequence that is an alteration in one or more letters of the genetic alphabet (A, T, C, G) that is present in at least 1% of the population. Scientists call such variations polymorphisms. Most polymorphisms are harmless and are part of normal human genetic diversity. However, others may increase the risk for disease and contribute to aging.

**Genetic code:** The four bases of DNA combine in a specific manner to spelling out a 'three-letter code'. This genetic code is carried by individual genes to instruct the specific proteins that are made by the cell. For example, the hemoglobin gene contains its specific genetic code which instructs the cell to produce the hemoglobin protein.

**Genome:** The complete physical and informational content of our DNA is referred to as the human genome. See Base (above) for the relationship between DNA, gene, chromosome and human genome.

**Genomics:** The branch of science that studies the structure, informational content and variation in the human genome is referred to as genomics.

**Lipoproteins:** When proteins combine with lipids, they are referred to as lipoproteins. Lipoproteins, which include HDLs and LDLs, are the principal means by which lipids are transported in the blood.

**Macrophage/Foam cell:** Macrophages are scavenger cells. A lipid-laden macrophage is called a foam cell/

**Metabolism:** Natural processes by which food is transformed into energy and its cellular waste products are eliminated.

**Mitochondria:** Organelles within cells that produce chemical energy (in the form of ATP) from the nutrients we consume.

**Nucleotide:** See Base above.

**Nucleus:** The central compartment with the cell that holds the human genome in the form of chromosomes.

**Nutrigenetics™:** The new field of applying SNP testing to help guide personalized formulations for the optimal combination of nutrients and vitamins, matched to an individual's unique genetic make-up is called Nutrigenetics.

**Oxidative Stress:** The chemical state in which the environment within cells becomes highly 'oxidized' and contains an excess of free radicals (see Free Radical above). Free radical can attach themselves to proteins and DNA inside the cell and cause damage. Oxidative stress is linked to many diseases and aging.

**Pharmacogenetics:** The new field of SNP testing aimed at providing individualized medicine is called Pharmacogenetics.

**Physiologic Health:** The body's ability to control oxidative stress and eliminate toxins and cholesterol etc.

**Polymorphism:** See Gene Variation above.

**Proteins:** Specific combinations of the 20 amino acids (see Amino Acids above) form tens of thousands of proteins that give the human body its form and function. Some proteins serve solely as the enzymes that are responsible for metabolism and DNA replication.

**ROS (Reactive Oxygen Species):** Free radicals are often referred to as reactive oxygen species (ROS), when molecular oxygen carries an extra electron. See Free Radicals.

**SNP:** "Single Nucleotide Polymorphism" and is pronounced 'snip'. These are natural genetic variations in our DNA that are largely responsible for why humans differ from one another. There are 3 million SNPs in our DNA.

**SNP Frequencies:** The degree to which a SNP occurs in a human population. The frequency of all SNPs is greater than 1%.

**Toxins:** Harmful substances that can be produced by the body, or pathogens or introduced from the environment. Environmental toxins can be introduced by ingestion, breathing or through the skin. Health is dependent upon cellular enzymatic detoxification systems to clear these harmful chemicals from our bodies. Inefficient clearance of toxins can lead to a variety of illnesses and diseases.

**Vitamins:** Organic nutrients that are essential for normal metabolism, growth and general health. They are required to activate specific enzymes. In addition, some enzymes can defend against oxidative stress by eliminating free radicals.

## Contributors

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**Roger Kendall, Ph.D.** is the Vice President of Research and Development for FoodScience Corporation and received his Ph.D. in Organic Biochemistry from Penn State University. He has worked for over 25 years in the field of nutritional research focusing on the role of nutrients as immune modulators, antioxidants and metabolic enhancers that promote healing and optimum health. He is considered to be the leading expert in the biochemistry and therapeutic applications of N,N-Dimethylglycine (DMG) and the Perna Canaliculus green lipped mussel.