



Gene SNP™

DNA Analysis

The New Fields of Nutritional Genetics and Epigenetics

Based on the latest science from the discovery of the entire human genome, health professionals can now apply new knowledge to offer customized nutritional recommendations to individuals based on genetic variations and lifestyle. In fact, health professionals will routinely identify what nutritional and lifestyle approaches are best for their clients to maximize optimal health.

Health professionals have appreciated for decades that some patients respond differently to specific nutritional interventions or supplements than others. What health professionals did not know is why these individual differences existed. That mystery is being clarified with the new field of nutritional genetics. Nutritional genetics refers to identifying specific genetic variations in individuals to determine differences in gene expression, enzyme function and so forth as it relates to nutrition. This information is communicated to the client in order to recommend specific nutrition and nutraceutical choices.

Nutritional genetics is based on the tenet that nutrients, whether ingested into or lacking from one's body, can have a direct effect on gene expression. In addition, a new term, epigenetics, has made its way into the nutritional genetics lexicon. Epigenetics refers to how a person's overall environment – including exercise, environmental exposures and nutrition – plays a distinct role in gene expression.

The Link Between Genes and Health

Genes, through the proteins they encode, determine how efficiently we metabolize foods, how effectively we detoxify harmful substances, and how we respond to certain conditions, among other functions. It is now known that there are many genetic variations in human populations. When a gene contains a variation (a change from the reference or native state), the protein encoded by that gene may be altered. That genetic alteration can be adaptive/beneficial or maladaptive. Such genetic variations that result from one nucleotide change in the DNA sequence are referred to as single nucleotide polymorphisms (SNPs).

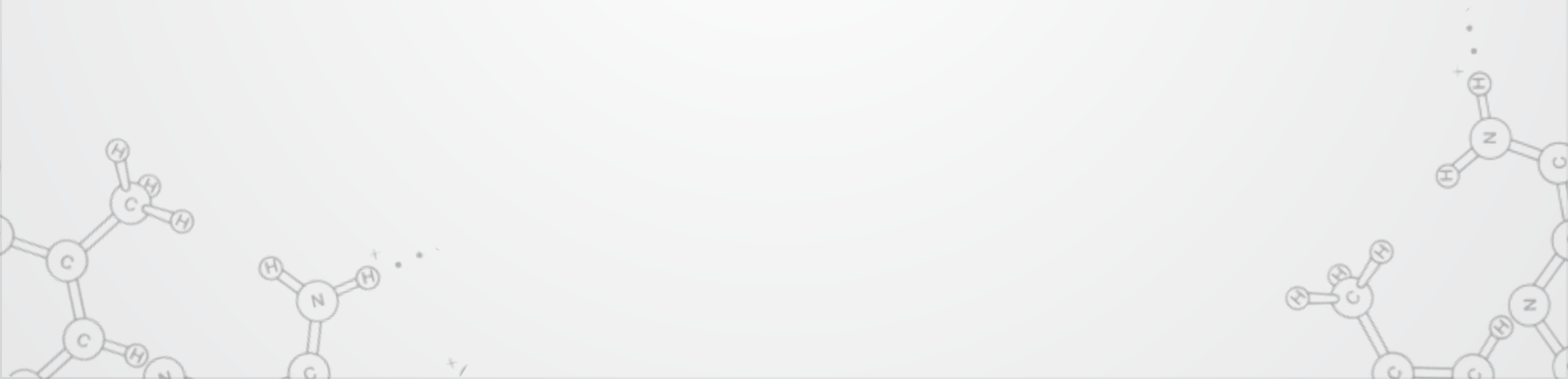
The Gene SNP™ DNA Analysis by nutraMetrix® offers the health professional a nutritional/epigenetic genetic program that is straightforward, comprehensive, affordable and cutting edge.

With a simple buccal smear, single nucleotide polymorphisms will be uncovered for many important genes. An Online Customer Profile, along with the DNA analysis, will generate an easy-to-read and easy-to-access online Health Action Plan.

Your patient's comprehensive Health Action Plan will not only provide information regarding their genetic makeup, but recommendations specifically tailored to optimize their diet, lifestyle, physical activity and nutraceutical supplementation.

This document will help you, the health professional, offer specific recommendations and guidelines to maximize your patient's well-being. As your patient progresses in his/her wellness plan, he/she can make changes to his/her Online Customer Profile and receive an updated Health Action Plan with new recommendations based on a new, healthier lifestyle.

From heart health to bone health, detoxification to antioxidation, nutrition to lifestyle, Gene SNP DNA Analysis will help you provide patients the answers they seek. In the next several pages, you will discover nutraMetrix's exciting Gene SNP DNA Analysis program.



▶ DETOXIFICATION

BIOCHEMICAL FOCUS

When potentially toxic compounds are ingested, inhaled or absorbed through the skin, they are removed from the body in a series of detoxification reactions generally divided into two phases.

Phase I Detoxification

The enzymes involved at this stage are known as activators; they activate the substance that needs to be removed, allowing the next phase to proceed. They work by attaching a single oxygen or nitrogen atom to the toxic compound. Many of these enzymes are cytochrome P-450s, which are mixed function oxidases.

Phase II Detoxification

The enzymes at this stage are called excretors because they catalyze synthetic reactions leading to the excretion of toxins from the body. For example, these enzymes bind the compound glutathione to the toxins activated in Phase I, making these potentially harmful substances water-soluble so that the body can remove them in urine or sweat. This test screens for variations of three Phase II genes, in the Glutathione S-Transferase family:

- *GSTM1*
- *GSTT1*
- *GSTP1*

Variations in these genes can affect the rate at which toxins are removed from the body.

► NUTRITIONAL & LIFESTYLE ADVICE

LIFESTYLE FOCUS

Tobacco

The findings on the negative effects of smoking can be best summed up by quoting former Surgeon General C. Everett Koop in his address to the Senate in 1998:

“Abundant evidence has established the causal relationship between the use of tobacco and cancer, cardiovascular disease, chronic obstructive lung disease, peripheral vascular disease, stroke, and a variety of serious pediatric maladies in children exposed to environmental tobacco smoke. These illnesses are so severe that nearly one of every five deaths in the U.S. is attributed to tobacco.”

Body Weight

The body mass index, or BMI, evaluates your weight in relation to your height. A healthy BMI ranges from 18.5 to 25; people with a BMI of 25 to 30 are classified as overweight; people with a BMI of 30 or higher are considered significantly overweight.

BMI, however, is not an absolute measure. Some adults in the healthy BMI range may have lots of fat and little muscle, which is not a healthy situation. On the other hand, people who have lots of muscle and little fat may not be overweight even if they have a high BMI.

There are many BMI calculators on the Internet, including one at the National Heart, Lung and Blood Institute:

<http://www.nhlbisupport.com/bmi/bmicalc.html>

Physical Activity

Physical activity that improves cardio-respiratory fitness – running, walking, aerobics, swimming and cycling – has been shown to reduce the risk of obesity and of numerous disorders, including heart disease, high blood pressure, type 2 diabetes and certain cancers.

Activity doesn't need to be strenuous to have a beneficial impact on health. United States health authorities recommend that all adults get at least 30 minutes of moderate physical activity a day – preferably every day. People trying to maintain a healthy weight after weight loss are advised to be even more physically active.

▶ HEART HEALTH

NUTRITIONAL FOCUS

B Vitamins

B vitamins are important in the most fundamental of metabolic processes in the human body. These vitamins – including folate (known as “folic acid” in synthetic form) and vitamins B6 and B12 – promote the normal production of new DNA for cells that are constantly growing and renewing themselves, such as skin, intestinal and blood cells. In addition, folate contains an important component that can affect gene expression and support normal DNA repair. Although vitamins are required by the body in only tiny amounts, these substances are crucial for normal metabolism. Studies show that the average American diet is deficient in many B vitamins.

A shortage of certain B vitamins can cause a substance called homocysteine to build up in your blood. According to medical research, a recommended amount of B vitamins helps support cardiovascular health, promotes healthy blood cells, and supports a healthy nervous system.

- Folate, B6 and B12 are water-soluble vitamins; they can be destroyed by heat and cooking. Keep cooking time to a minimum and prepare foods rich in these vitamins by steaming, microwaving or stir-frying.
- Drinking alcohol reduces the benefits of B vitamins. Keep alcohol consumption within the recommended limits. The U.S. Department of Health & Human Services defines a moderate alcohol intake as no more than one drink per day for women and no more than two drinks per day for men.

Food Sources

- *Folate: liver, leafy vegetables, citrus fruit, whole grains, wheat germ, avocados*
- *Vitamin B6: poultry, pork, eggs, beans, legumes, whole grains, sunflower seeds*
- *Vitamin B12: liver, kidney, red meat, poultry, fish, eggs, soy powder, yeast extracts*

► HEART HEALTH

DIETARY & LIFESTYLE FACTORS RELEVANT TO HEART HEALTH

- *Folate*
- *Vitamin B6*
- *Vitamin B12*
- *Fruits and vegetables*
- *Antioxidants*
- *Refined carbohydrates*
- *Saturated fat*
- *Cholesterol*
- *Omega-3 fatty acids*
- *Tobacco*
- *Body weight*
- *Physical activity*

Lipid and cholesterol metabolism: When certain variations of the genes determining cholesterol metabolism are identified, individuals may be advised to reduce consumption of saturated fats and cholesterol, replacing them with unsaturated fats in their diet.

B vitamin genes: If the enzymes in the B vitamin pathway are present in the form that decreases their effectiveness, we recommend increasing consumption of folate, vitamin B6 and vitamin B12 and taking the recommended supplement.

Antioxidant genes: After screening the MnSOD and SOD3 genes, the analysis will indicate whether the form of either gene indicates a decrease in overall antioxidant activity; if so, we recommend increased consumption of antioxidants through food and supplementation. We also recommend avoidance of active and passive (secondhand) smoke.

Inflammatory responses: For individuals with variations in the IL-6 gene, that may result in altered inflammatory responses, we recommend increased consumption of antioxidants.

Insulin sensitivity: Individuals with a deletion in the ACE gene are advised to reduce their intake of refined carbohydrates and simple sugars, and to focus on increasing unrefined complex carbohydrates in their diet. They are also advised to maintain a healthy weight and to engage in regular physical activity.

► BONE HEALTH

DIETARY & LIFESTYLE FACTORS RELEVANT TO BONE HEALTH

- *Calcium*
- *Vitamin D*
- *Caffeine*
- *Body weight*
- *Physical activity*

The main determinants of peak bone mass are genetic factors, early life nutrition, diet and exercise. Of the nutritional factors, calcium and vitamin D are the most important contributors to peak bone mass. Some of these factors may interact; for example, low dietary intake of calcium in addition to an altered VDR gene may result in low peak bone mass.

Individuals with certain variations of “bone health” genes have an increased requirement for calcium and vitamin D, which are needed to maintain bone health and healthy bone mass. It is vital that these individuals include plenty of calcium-rich foods in their diet, as well as foods rich in vitamin D.

Certain variations in “bone health” genes make the bones less tolerant of caffeine. It is important that individuals with these variations keep their caffeine consumption to a minimum, below the recommended upper limit of 300 milligrams a day.

If the person’s “bone health” genes contain variations that negatively affect bone mineral density, being underweight adds additional risk. This is because bones are strengthened when they have a load to bear, and people who are small-boned (or underweight) do not have the ongoing benefit of such strengthening. Underweight people need to ensure that they consume all the necessary nutrients for good bone health and exercise regularly.

For people who have certain variations in their “bone health” genes, it is of great importance to incorporate weight-bearing exercises – such as walking, running and aerobics – into their regular exercise program. If bones are known to be weak, all exercise should be done under the supervision of a specially trained health professional.

▶ ANTIOXIDATION

DIETARY & LIFESTYLE FACTORS RELEVANT TO ANTIOXIDANTS

- *Fruits and vegetables*
- *Antioxidants*
- *Tobacco*

If the DNA analysis indicates that the enzymes produced by antioxidant genes are expected to be in their ideal location and have normal activity, we recommend a diet with a healthy variety of antioxidant-rich fruits and vegetables for optimum health. The GST family of genes also contribute antioxidant activity; an absence of variations in these genes indicates that they should be functioning effectively.

If the DNA analysis indicates that the enzymes produced by the antioxidant genes are either not expected to be in their ideal location or have reduced activity, we recommend increased antioxidant consumption to support antioxidant activity in the body, along with avoidance of tobacco smoke. When considering the GST family of genes, we focus on consumption of cruciferous and allium vegetables.

NUTRITIONAL FOCUS

Antioxidants

Fruits and vegetables are regarded as the best source of dietary antioxidants; numerous studies have proven that a high intake of fruits and vegetables promote cardiovascular and overall health. An ideal intake includes a minimum of three to four portions of vegetables and at least three portions of fruit daily, including at least one portion of citrus fruit.

In addition to fruits and vegetables, common foods particularly high in various antioxidants are soy products (tofu, tempeh, soy milk, yogurts and cheese), green and black tea, garlic and red wine, which has beneficial health effects if consumed in moderation.

Food Sources

Below are several sources of foods rich in major antioxidants:

- *Vitamin A: eggs, milk, cheese, cream, meat, liver, kidney beans, cod, halibut, fish oil*
- *Vitamin C: citrus fruit, kiwi fruit, strawberries, tomatoes, alfalfa sprouts, green peppers*
- *Vitamin E: wheat germ, corn, nuts, seeds, olives, spinach, green leafy vegetables*

Introduction to Gene Variations and their Significance

The following table summarizes the genes and the variations that are analyzed with the nutraMetrix® Gene SNP™ DNA Analysis. Some gene variations are true SNPs – representing single nucleotide changes from a native state (as explained in the introduction). Other variations may be insertions of nucleotide sequences that may alter the resulting protein. In some cases, deletions of gene sequences or even entire genes are revealed. Only those gene variations that have a consequence on nutritional or health status and that can be affected by lifestyle changes, diet and nutrition are included.

Genetic variations that are diagnostic of disease states (i.e. sickle cell anemia, Tay Sachs, Cystic Fibrosis, etc.) are NOT part of the nutraMetrix Gene SNP DNA Analysis.

Tips on Reading the Table:

On the left column, the gene that codes for a particular protein is stated.

The next column reveals the specific variation that is screened for that gene.

The last column discusses how the particular variant can have an impact on one's health.

Example 1:

The CBS (Cystathione Beta Synthetase) gene is screened for the variation 699C>T. The “T” at the end indicates that thymine is substituted for cytosine “C” at the 699th position of that gene. That one nucleotide change at that specific location can have an impact on health, as noted on the third column.

Example 2:

The ADH1B (Alcohol Dehydrogenase 1B – Cytosolic) gene is screened for two variations. The first variation screened is Arg369Cys. That indicates that the amino acid cysteine has been substituted for the amino acid arginine at the 369th position of the protein coded for that gene. The resulting impact on health is noted on the third column.

Example 3:

The ACE (Angiotensin Converting Enzyme) gene is screened for two variations (from the reference or native state) – an insertion of a nucleotide sequence and a deletion. Each particular variant's impact on one's health is discussed in the third column.

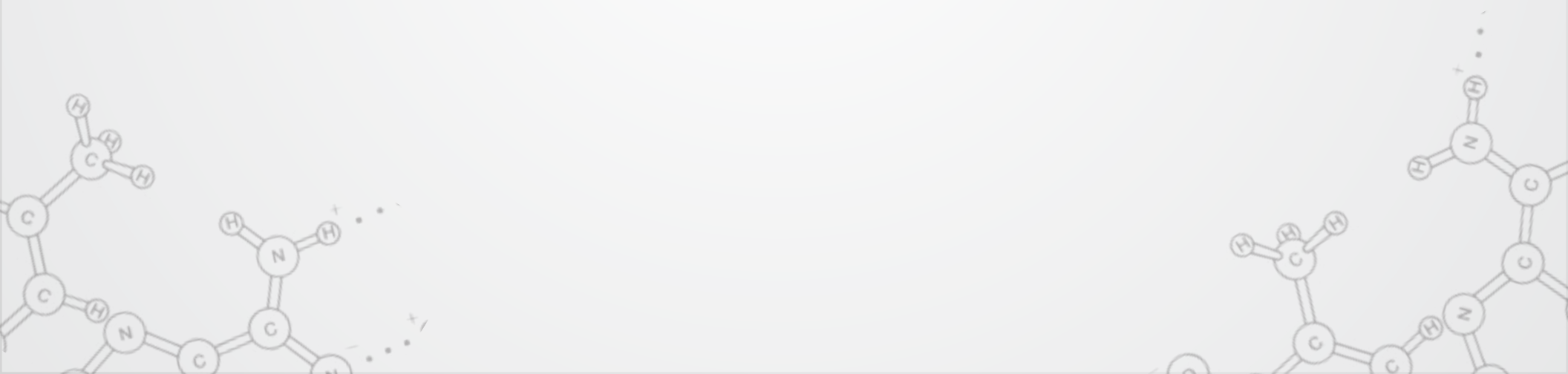
Example 4:

The VDR (Vitamin D Receptor) gene is screened for three variations. Taq1 indicates a nucleotide change within the gene that affects the recognition site of a restriction enzyme known as Taq1.

Final Remarks:

The nutraMetrix® Gene SNP™ DNA Analysis serves as your guide to offer nutritional genetics in your practice. As a health professional, you may further modify and/or enhance the recommendations as you see fit for your particular patient.

Your role as a nutraMetrix Health Professional using the Gene SNP DNA Analysis is to use this information as a tool to customize lifestyle, nutritional and nutraceutical recommendations for the benefit of your patients. Clear communication, coaching and following-up with these lifestyle, nutrition and nutraceutical recommendations will result in maximal compliance and better results. Your patients will continue to appreciate these recommendations for a lifetime while enhancing your own professional satisfaction on a whole new level.



Genes	Genetic Variation Screened For	Impact on Health
ACE (Angiotensin Converting Enzyme)	Insertion	Variant has lower ACE activity. Lower or inhibited ACE activity has been associated with better muscle mass, use and retention. This variant appears to have an enhanced metabolic efficiency. Appears to be good for endurance-related exercises.
	Deletion (In Intron 16)	Variant has higher ACE activity. This variant has been associated with increased risk of high blood pressure (hypertension), decreased insulin sensitivity, and altered levels of total cholesterol and plasma triglycerides. Exercise and a healthy diet can help reduce body mass index (BMI), blood pressure and improve insulin sensitivity.
ADH1B (Alcohol Dehydrogenase 1B) - Cytosolic	Arg369Cys	Variant has increased ADH enzyme activity which results in rapid conversion of alcohol/ethanol to acetaldehyde. Due to this rapid conversion, variant can experience flushing, nausea and a rapid heart rate caused by build up of acetaldehyde. These negative reactions to alcohol have a tendency to affect alcohol consumption (reducing it). This variation appears to give a reduction in the risk for alcoholism and cancers related to excess alcohol consumption.
	Arg47His	Variant has increased ADH enzyme activity which results in rapid conversion of alcohol/ethanol to acetaldehyde. Due to this rapid conversion, variant can experience flushing, nausea and a rapid heart rate caused by build up of acetaldehyde. These negative reactions to alcohol have a tendency to affect alcohol consumption (reducing it). This variation appears to give a reduction in the risk for alcoholism and cancers related to excess alcohol consumption.
ADH1C (Alcohol Dehydrogenase 1C) - Mitochondria	Ile349Val	Variant has increased ADH enzyme activity which results in rapid conversion of alcohol/ethanol to acetaldehyde. Due to this rapid conversion, variant can experience flushing, nausea and a rapid heart rate caused by build up of acetaldehyde. These negative reactions to alcohol have a tendency to affect alcohol consumption (reducing it). This variation appears to give a reduction in the risk for alcoholism and cancers related to excess alcohol consumption.
ADRB2 (Beta-2 Adrenergic Receptor)	Gln27Glu	Variants may have reduced VO2 max which does reduce the time to fatigue and can affect recovery time. Females have reduced fat oxidation during exercise, higher BMI, and higher fat mass. Males, if obese and sedentary, have higher increase in fat accumulation. If not obese or obese but exercising, have reduced ability for fat loss.
	Gly16Arg	Variant has been associated with better performance in endurance activities. Has a tendency for higher VO2 max levels which can improve with training.
AGT (Angiotensinogen)	Met235Thr	Variant has higher levels of angiotensinogen, which has been associated with a higher risk of high blood pressure (hypertension). Regular, moderate intensity exercise, coupled with a healthy diet low in sodium/salt, appears to help reduce BP.
ALDH2 (Aldehyde Dehydrogenase 2)	Glu 487Lys	Variant has decreased activity of aldehyde dehydrogenase 2 enzyme (located in mitochondria), which is necessary to transform acetaldehyde to acetic acid. Due to decrease in enzyme and enzyme activity, variant has decreased ability to metabolize alcoholic drinks/ethanol, deficiency of enzyme leads to flushing and other vasomotor symptoms caused by build up of acetaldehyde. These negative reactions to alcohol have a tendency to affect alcohol consumption (reducing it). This variation appears to give a reduction in the risk for alcoholism related to excess alcohol consumption.
APOC3 (Apolipoprotein C-III)	3175C>G	Variant is associated with higher plasma levels of APOC3, possibly leading to increased levels of cholesterol and plasma triglycerides. A diet low in cholesterol, saturated fats and trans fats but rich in monounsaturated fats is important for both variants and nonvariants.
CBS (Cystathionine Beta Synthase)	699C>T	Variant may have an increase in CBS enzyme activity, which may lead to lower plasma homocysteine levels.

Genes	Genetic Variation Screened For	Impact on Health
CETP (Cholesterol Ester Transfer Protein)	279G>A	Variant appears to have lower CETP levels, resulting in lower LDL and VLDL levels, with higher HDL levels; overall, variant appears to have better lipid/cholesterol profiles than nonvariant. This does not mean either the variant or nonvariant have good or bad lipid/cholesterol issues. Exercise and a diet low in cholesterol, saturated fats, and trans fats is important for both variant and nonvariant. Nonvariants have a better response for reduction in lipid/cholesterol when exercising.
COL1A1 (Collagen Type 1 Alpha)	2046G>T	Variant has been associated with reduced COL1A1 activity resulting in reduced bone mass density and a 50-60% increased risk of developing osteoporosis. COL1A1 encodes the major component of Type I collagen, the fibrillar collagen found in most connective tissues, and the only component of the collagen found in cartilage. Variant has an altered ratio of procollagen chains/strands, leading to a reduced or weakened Type I collagen in bone, resulting in reduced bone strength and increased fragility.
CRP (C-Reactive Protein)	(-732)A>G	Variant has been associated with lower levels of CRP. Higher CRP levels are associated with inflammatory response. Variant has been associated with better performance in endurance activities. Has a tendency for higher VO2 max levels, which can improve with training.
	1059G>C	
	219G>A	
CYP1A1 (Cytochrome P450, Subfamily I, Aromatic Compound-Inducible (Subfamily A), Polypeptide 1)	Ile 462Val	Variant has increased CYP enzyme activity, which can lead to an excess of genotoxic intermediates. Genotoxic substances are known to be potentially mutagenic or carcinogenic, contributing to genetic mutation and the possible development of tumors. Variant has been associated with increased risk of developing lung and colon cancer (CRC). Variant should avoid well-done meats, smoking and being around smoke, while increasing consumption of leafy and cruciferous vegetables.
CYP1A2 (Cytochrome P450, Subfamily 1, Aromatic Compound-Inducible (Subfamily A), Polypeptide 2)	1F	Variant has reduced CYP enzyme activity. CYP1A2 is involved with the metabolism and elimination of prescription drugs, coffee/caffeine, and cigarette smoke toxins. Variant has been associated with an increased risk of myocardial infarction (MI), pancreatic cancer, lung cancer, and colon cancer (CRC). Variant should avoid smoking, while reducing coffee/caffeine, red meat (well-done) and pan fried meat.
GSTM1 (Glutathione-S-Transferase)	Present or Deletion	Variants may have reduced VO2 max, which does reduce the time to fatigue and can affect recovery time. Females have reduced fat oxidation during exercise, higher BMI, and higher fat mass. Males, if obese and sedentary, have higher increase in fat accumulation. If not obese or obese but exercising, have reduced ability for fat loss.
GSTT1 (Glutathione-S-Transferase)		Variant has a reduced protection against harmful oxygen radicals, toxins, and carcinogens. May have increases in inflammation, muscle/joint pain, and shortened time to fatigue. Variant, due to deletion of GSTT1, has reduced protection (Phase II detox) against harmful oxygen radicals, toxins and carcinogens.
GSTP1 (Glutathione-S-Transferase)	Ile 105 Val	Variants have changes in the structure of the GSTP1 enzyme, which results in decreased enzyme activity. Variants have reduced protection against harmful oxygen radicals, toxins and carcinogens.
	Ala 114 Val	

Genes	Genetic Variation Screened For	Impact on Health
IL-6 (Interleukin 6)	(-634) G>C	Variant has an increased expression of IL-6, which can result in increased inflammation, slower muscle tissue recovery and repair after exercise, increased soft tissue damage with inadequate recovery time between workouts, and increased possibility of joint pain.
	(-174) G>C	
LIPC (Hepatic Lipase)	-293 G>A	Promoter variant is associated with low rates of insulin-stimulated whole-body nonoxidative glucose disposal and with low rates of insulin-stimulated whole-body glucose oxidation in FCHL family members. Also associated with high levels of fasting insulin, VLDL, LDL in familial combined hyperlipidemia (FCHL) family members. Associated with low HDL and high LDL.
	(-557) C>T	Variant is associated with three other base variants in the proximal LIPC promoter. T allele leads to diminished hepatic lipase (HL) promoter activity and associated with 15-30% lower post-heparin HL activity. HL deficiency generally associated with increased coronary artery disease (CAD). Those with T allele may only have problems with increased CAD when they also have low cholesterol ester transfer protein (CETP) activity (variant B2/B2).
LPL (Lipoprotein Lipase)	Ser474Stop	Variant has an increased LPL level. This is considered a gain of function variant, which provides for reduced triglyceride and LDL level, and higher HDL levels; overall, variants appear to have better lipid/cholesterol profiles than non-variants. Variant may have increased protection against high blood pressure (hypertension). Physical exercise upregulates LPL expression in muscle to provide increased fatty acids availability to accommodate increased energy requirements. Exercise and a diet low in cholesterol, saturated fats and trans fats, but rich in unsaturated fats, is important for both variants and non-variants.
MTHFR (Methyl-enetetrahydrofolate Reductase)	Ala 222 Val	Variants have reduced MTHFR enzyme activity which, is linked to increased homocysteine levels resulting in higher rates of heart disease, pulmonary embolism, stroke and deep vein thrombosis. For variants and non-variants, intense exercise appears to raise homocysteine levels when folic acid and vitamin B12 levels are low, while regular, routine exercise appears to reduce homocysteine levels.
	Glu 429 Ala	
MTR (Methionine Synthase)	Asp 919 Gly	Variant has increased MTR enzyme activity, which appears to help reduce levels of homocysteine in some cases, while in others it may have the opposite effect. Research on this SNP is inconclusive.
MTRR (Methionine Synthase Reductase)	Ile 22 Met	Variant has reduced MS_MTRR enzyme activity which has been linked to an increased risk of cardiovascular disease and possibly a moderate increase in homocysteine level.
NOS3 (Nitric Oxide Synthase)	Glu 298 Asp	Variant has decreased nitric oxide (NO) production. NO improves blood flow by acting on smooth muscles allowing these to relax and thereby improving vasodilation. Due to decrease in NO, variants may be more prone to atherosclerotic plaques and increased blood pressure (BP). Variants should not smoke. While exercising, NO appears to help by improving the flow of oxygenated blood to working muscles and by improving the utilization of oxygen in order to increase energy production. Due to decrease in NO, variants may have decreased endurance and increased blood pressure (BP). Exercise appears to augment NO release which can help to improve BP and endurance/muscle use over time.

Genes	Genetic Variation Screened For	Impact on Health
PON1 (Paraoxonase 1)	Gln192Arg	Variant has lower PON1 activity, resulting in a higher rate of LDL oxidation by free radicals. Oxidized LDL is believed to be the key mediator of atherosclerosis and coronary artery disease (CAD). Variant has been associated with increased risk of cardiovascular disease (CVD) and myocardial infarction (MI). Dietary and supplemental polyphenols (berries/fruits) and antioxidants (tomato juice, lycopene) can be beneficial in reducing the oxidation of LDL.
	Leu55Met	Variant affects the binding specificity of the substrate. In association studies, the non-variant, Leu55 has been associated with increased risk for Type II diabetes. It has been reported that the Leu homozygous (Leu/Leu) and heterozygous (Leu/Met) variant are independent risk factors for coronary heart disease.
PPARY2 (Peroxisome Proliferators-Activated Receptor Gamma)	Pro12Ala	Variant has been associated with improved insulin sensitivity, higher levels of HDL, and better weight loss with exercise. Beneficial effects of variant appears to depend on BMI and body fat; those with higher BMIs (body fat) appear to have minimal or no benefits. Exercise and a healthy diet good for variants and non-variants.
PPARGC1A (Peroxisome Proliferative Activated Receptor, Gamma, Coactivator 1, Alpha)	Gly 482 Ser	Variant will have a smaller increase in VO2 max and insulin sensitivity than those without variation when exercising. May have shorter time to fatigue and therefore reduced endurance than those without variation. May have higher resting glucose and insulin resistance (has been associated with type 2 diabetes). Exercise and diet improves profile.
SOD2 (Manganese Superoxide Dismutase)	Ala 16 Val	Variant has been associated with decreased MnSOD antioxidant protection within the mitochondria, but increased protection within the cell. Non-variant and variant with CT, due to having more MnSOD concentrated in mitochondria, has decreased antioxidant protection outside of mitochondria. Dietary antioxidant sources can be beneficial in reducing the affects of free radicals.
SOD3 (Copper, Zinc Superoxide Dismutase)	Arg 231Gly	Variant SOD3 enzyme has a loss of affinity for heparin, resulting in the release of active SOD3 from tissues and blood vessels at an advanced rate. Consequently, antioxidant protection could be reduced at certain locations.
TNF-Alpha (Tumor Necrosis Factor-Alpha)	(-308) G>A	Variant has an increased level of TNF-alpha which can result in increased inflammation, slower muscle tissue recovery and repair after exercise, increased soft tissue damage with inadequate recovery time between workouts, and increased possibility of joint pain.
VDR (Vitamin D Receptor)	Bsm1	Variant has been associated with higher fasting glucose and lower insulin sensitivity. May be associated with greater body weight and better bone formation and retention with exercise. Variants appear to have better strength at baseline; may see better strength gain with weight training.
	Fok1	Variant appears to be associated with lower VDR transcriptional activity, higher fasting glucose levels, and higher plasma insulin levels. May be associated with greater body weight. May have improved bone mass density (BMD) with exercise. May be associated with strength.
	Taq1	May have improved bone mass density (BMD) with exercise.