Health & Wellbeing

YOUR PERSONAL GENETIC PROFILE

GENETIC PROFILE ID # 3000041

POWERED BY fitgenes

Introduction

Thank you for choosing a Fitgenes program to assist in maximising your health potential.

This report contains your personal genetic profile showing any variants you may have in a series of genes, especially selected as they can influence your health and longevity, and impact your optimum nutrition and fitness level. This information, combined with various health and lifestyle assessments, is used by your Fitgenes Accredited Practitioner to design more personalised and targeted nutrition, exercise and lifestyle interventions. Your Personal Genetic Profile is an important piece in the puzzle helping you maximise your potential for Healthy Living and Healthy Ageing.

UNDERSTANDING NUTRIGENETICS AND NUTRIGENOMICS

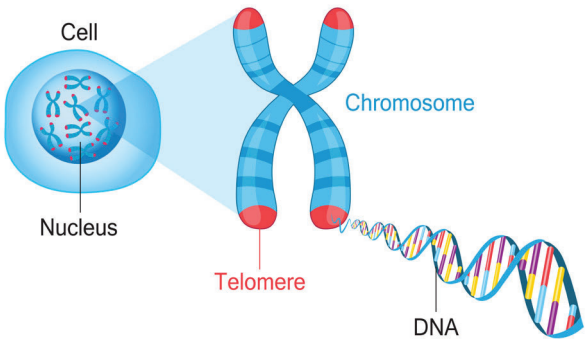
Nutrigenetics and nutrigenomics are the disciplines focused on the link between diet and genes. In particular, nutrigenetics is the science that studies genetic variants associated with differential response to nutrients, as well as our health and wellbeing, while nutrigenomics is a whole system approach that investigates how nutrients can affect gene expression. Other lifestyle choices, including exercise, can also affect gene expression.

It's true that you can't change your inherited genes, however you can compensate for their influence by choosing better lifestyle choices that match your genes. A good computing analogy is that, in essence, nutrigenetics determines your body's hardware and nutrigenomics determines the software i.e. the messages that are sent out. In short, gene expression is modifiable; **your genes do not necessarily control your destiny**, you can modify gene expression and improve the functioning of your genes by making the right nutrition, exercise, and other lifestyle choices.

THE BASICS OF DNA

The human genome consists of 23 pairs of chromosomes found in the cell nuclei, as well as mitochondrial DNA, which contain genes and other non–coding sequences. Overall, it is estimated that each individual has approximately 30,000 genes. A gene is, essentially, a sequence of DNA that codes for a molecule with a function. As chromosomes come in pairs, each individual has two copies of each gene, one inherited from each parent.

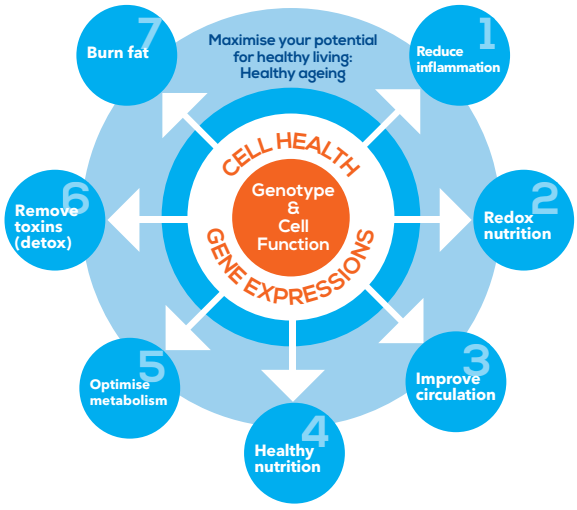
Genetic variants (alterations in the DNA sequence) is what makes everyone unique, but also contributes to your health status.



LIFE EXPECTANCY VERSUS HEALTH EXPECTANCY

Globally, healthcare systems are facing major challenges as world is in the midst of an epidemic of preventable lifestyle diseases, such as obesity, diabetes, and heart disease. As well as having this epidemic, we have an ageing population. Consequently, **even though life expectancy has increased, health expectancy is decreasing**.

Historically, the major factors contributing to the decline in health expectancy have been: lack of appropriate exercise, food quality and quantity, smoking, alcohol and/or drugs, stress, and environmental factors such as air and water pollution, use of chemicals in the home. However, now one of the most important factors is: **interaction of your genes with your diet and other lifestyle choices (D. J. Hunter, 2005).** As a consequence, nutrigenetics and nutrigenomics can be an important personalised tool to improve health.



FITGENES PERSONALISED GENOME–BASED HEALTH AND WELLBEING

Personalised healthcare requires information that is specific to the individual and not just 'one size fits all'. Since the human genome was sequenced in 2000, there has been an expectation that genetic testing would contribute towards the understanding to many medical issues. It has now been proved that **most human health issues have a genetic component (Peltonen & McKusick, 2001)**, but the ultimate phenotype depends on the interaction of genes with the environment i.e. lifestyle choices. For this reason, testing for **variants in key genes of major physiological pathways** provides the basis for personalised interventions before clinical symptoms appear. **In summary, the new era of personalised health and wellbeing is here.**

Fitgenes aims to help individuals reach their health goals and increase their health expectancy, maximising their potential for Healthy Living and Healthy Ageing, by applying nutrigenetics and nutrigenomics evidence.

Your Personal Genetic Profile

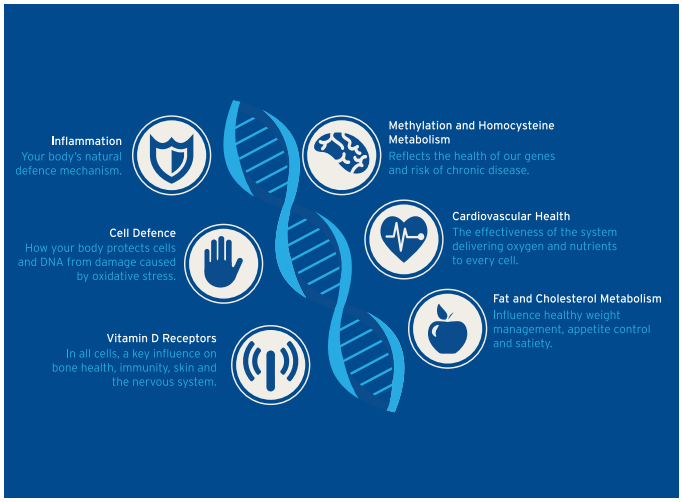
Fitgenes has designed your personal Genetic Profile Report to identify any of your variants in key genes of major physiological pathways that may influence the way your body functions, and how it responds to what you eat, how you exercise, and how you live your life, as well as your risk for a number of health issues related to these pathways.

The result of your genetic test can be either the reference variant (that found in the human reference genome) or the alternative (that other than the reference found at the same position). As described earlier, genes in every human being exist as a pair. Variants in one or both of the genes, known as alleles, may result in three possible physiological outcomes as listed in the following table. The potential risk variants of each gene (denoted by orange or red dots) indicate an impaired or suboptimal physiological functioning of the gene product.

Beneficial	Less Beneficial	Least Beneficial
One or both of the alleles in the gene pair contribute to the normal healthy functioning of the gene product.	One of the alleles in the gene pair is contributing to a situation that impairs the healthy functioning of the gene product.	Both of the alleles in the gene pair are contributing to a situation that impairs the healthy functioning of the gene product.

Historically, the most common variant has been the beneficial variant from a physiological point of view, compared with the alternative variant. However, with today's Western lifestyle, this may now be reversed. For example, the ability to store fat was an advantage when we were hunter–gatherers, whereas in today's obesogenic environment this can be a major disadvantage.

In order to simplify the understanding of your results, the genes tested as part of your profile have been grouped according to the primary physiological effect they have on your body, although it is possible that a gene has an effect in multiple groups. The groupings chosen are:



The major purpose of these groups is to help identify the focus area(s) for your nutritional, health and lifestyle interventions. A high number of 'less' or 'least' beneficial variants in a group is a 'Call to Action'. Once you have identified your primary focus group and completed any health and lifestyle surveys to identify your phenotype (your current health status), your Fitgenes Accredited Practitioner can recommend the appropriate interventions to help you reach your health goals.

NOTE 1: Different genetic testing companies can test different strands of the DNA i.e. some test the forward strand and some test the reverse strand. Therefore, when looking at scientific papers for specific genetic variants, it is important to know which strand they tested. For example, if the result from companies testing the forward strand for a specific variant is 'AG', it is the same result for testing companies testing the reverse strand who report the results as 'TC', as the base pairs are always A–T and C–G.

NOTE 2: In the results section when only one letter is reported i.e. 'A', then both are the same letter i.e. 'AA' in this case.

NOTE 3: Some genetic variants are 'palindromic'. That is, the alleles in the forward and reverse directions are the same as the base bases i.e. C–G for the forward strand and G–C for the reverse strand. Therefore, as per NOTE 1, it is critical to know which strand is being tested to identify the correct risk allele.

Disclaimer and limitations: all genes and variants presented in this report, with their corresponding implications for your health, have gone through extensive scientific literature review. Nevertheless, genetic research is rapidly increasing, and our understanding of the information included in this report will increase over time, and so the content of future reports may vary from this one. An extensive list of gene–specific references can be found in Pracware.

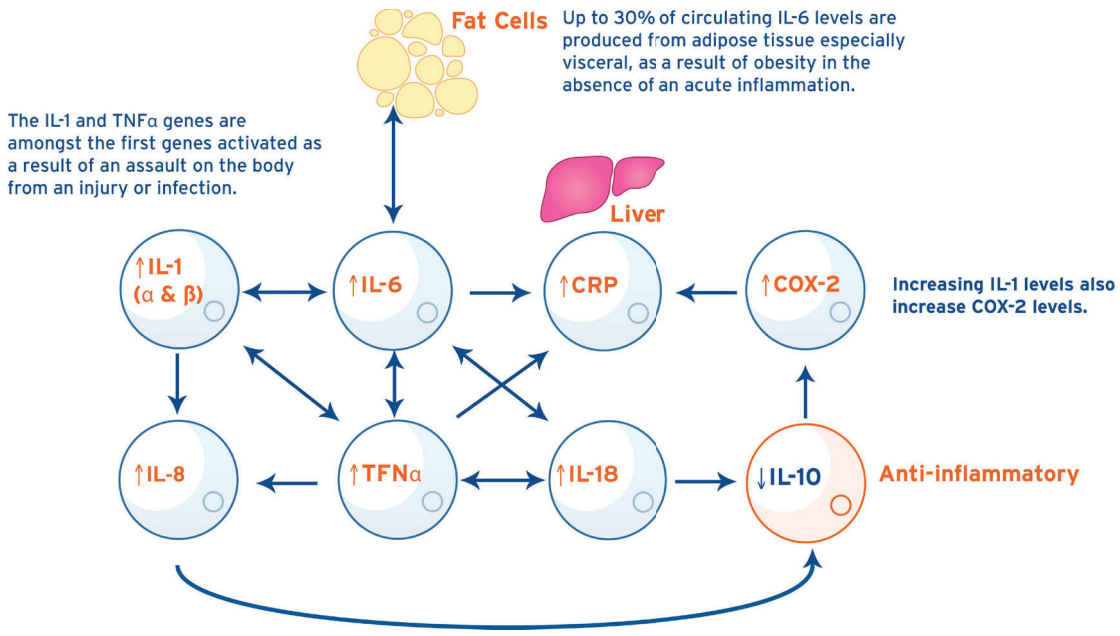
Genes that affect Inflammation

Inflammation is a natural body defence mechanism and an important part of the normal immune response; it protects you from infections and helps with tissue repair after an injury. Your health and wellbeing is critically dependent on this inflammatory response being well regulated and operating correctly.

Ideally, when you get sick or injured you want a strong inflammatory response that ensures you deal effectively with any infection or injury, but then settles down. You do not want an inflammatory response that is overly aggressive as this can lead to more inflammation, tissue destruction, muscle wastage, and bone loss. You also do not want a state of chronic inflammation. This is associated with many chronic diseases: cardiovascular disease, atherosclerosis, diabetes, periodontal disease and many autoimmune diseases (Franks & Slansky, 2012; P. Hunter, 2012; Lopez–Candales, Hernandez Burgos, Hernandez–Suarez, & Harris, 2017; Tuttolomondo et al., 2012; Van Dyke, 2008; Wellen & Hotamisligil, 2005). Genetically, some people are more likely to have an overly aggressive inflammatory response or chronic inflammation.

The inflammation process is controlled by an interplay between pro–inflammatory cytokines, which are a type of molecules that promote inflammation, and anti–inflammatory cytokines, which inhibit the synthesis of pro–inflammatory cytokines.

SIMPLIFIED INFLAMMATION BIOCHEMICAL PATHWAY



PRO-INFLAMMATORY CYTOKINES

#	Gene (variant)	Description of the encoded molecule	Your Result			
1	IL-1α-1 (rs1800587)	Key regulators of the pro-inflammatory responses to tissue injuries, as well as the promotion of fever and sepsis. Two forms of the IL-1 family of cytokines, IL1-α and IL-1β, which are produced predominantly in macrophages, play critical roles in many autoimmune diseases. IL-1 cytokines trigger IL-6, IL-8 and TNFα. Orange dot and particularly red dot indicate increased production of the IL-1 cytokines and increased risk of inflammation.	TC			
2	IL-1α-2 (rs17561)		GT			
3	IL-1-β (rs16944)		G			
4	IL-6 (rs1800795)	Increases in response to infection, trauma or stress. Associated with many auto-immune diseases. Body fat is a major source of IL-6. Main trigger of CRP. IL-6 can be both pro-inflammatory and anti-inflammatory, depending on biomarkers, such as waist circumference and body fat mass. Orange dot and particularly red dot indicate the highest IL-6 and CRP serum levels for most clinical applications and increased risk of inflammation, especially in Caucasian populations.	C			
5	IL-8 (rs4073)	Produced early in the inflammatory response and controls activity of white blood cells / neutrophils. Persists for weeks once released. Triggered by IL-1α, IL-1β and TNFα. Orange dot and particularly red dot indicate increased production of IL-8 and increased risk of inflammation.	TA			
6	IL-18 (rs1946518)	Triggers TNFα and decreases production of anti-inflammatory IL-10. Orange dot and particularly red dot indicate increased production of IL-18 and increased risk of inflammation.	GT			
7	TNFα (rs1800629)	Produced by the immune system to kill bacteria, viruses and parasites. Body fat releases TNFα. Triggers CRP, COX-2, IL-6, IL-1α, IL-1β and IL-8. Orange dot and particularly red dot indicate increased production of TNFα and increased risk of inflammation.	GA			
8	CRP-1 (rs2794520)	Acute phase protein, which is produced in the liver and fat cells, is an important indicator of chronic, systemic (body wide) inflammation. Although CRP is a key component of the human acute phase response, it is also expressed at low levels in apparently healthy individuals. CRP is triggered mainly by IL-6 and is associated with many chronic diseases. Orange dot and particularly red dot indicate increased production of CRP and increased risk of inflammation.	TC			
9	CRP-2 (rs2592887)		GA			
10	CRP-3 (rs1205)		CT			
11	COX-2-3 (rs689466)	Main enzyme that converts arachidonic acid into pro-inflammatory prostaglandins. COX-2 plays a key role in chronic inflammatory events such as pain response, infections, injuries, burns, trauma and fever. Orange dot and particularly red dot indicates increased production of COX-2 and increased risk of inflammation.	A			
12	COX-2-4 (rs5275)		CT			

ANTI-INFLAMMATORY CYTOKINES

#	Gene (variant)	Description of the encoded molecule	Your Result			
13	IL-10-1 (rs1800896)	Immune regulating and anti-inflammatory cytokine whose main function is to terminate the inflammatory signal in inflammatory cells such as macrophages. Therefore, the ability to produce IL-10 may be critical to the final outcome of an inflammatory response. IL-10 inhibits the pro-inflammatory IL-1α, IL-1β, IL-6, IL-8 and TNFα cytokines. Orange dot and particularly red dot indicate decreased production of IL-10 and increased risk of inflammation.	GA			
14	IL-10-2 (rs1800871)		TC			
15	IL-10-3 (rs1800872)		CA			

Genes that affect Cellular Defence

Your body continuously produces reactive oxygen species (ROS), one type of the molecules referred to as free radicals, as a natural by–product of the normal metabolism of oxygen. Elevated levels of these molecules can cause oxidative stress and damage your DNA, lipids and proteins. Oxidative stress leads to ageing and underlies all disease processes, including cardiovascular disease, dementia and diabetes, premature ageing and plays a role in the development of cancer (Devasagayam et al., 2004). Poor liver health, inflammation, diabetes, high cholesterol, obesity, environmental toxins, chemotherapy, radiation, and smoking will all increase free radical production and can lead to DNA damage.

Your body produces antioxidant enzymes which remove these ROS, which form the "primary anti–oxidant defence system". Some people are genetically predisposed towards insufficient production of these antioxidant enzymes and are therefore at higher risk of increased oxidative damage.

Exogenous anti–oxidants, such as vitamins C and E, carotenoids, and polyphenols derived from plant foods, form a dietary "secondary ant–oxidant defence system."

The optimum approach to minimising the risk of oxidative stress is to utilise your body's own powerful antioxidant enzymes by upregulating their production and, where necessary, compensating for potential impairments with nutritional and lifestyle interventions.

THE ANTIOXIDANT HIERACHY

Increasing protective effect with progress up the pyramid

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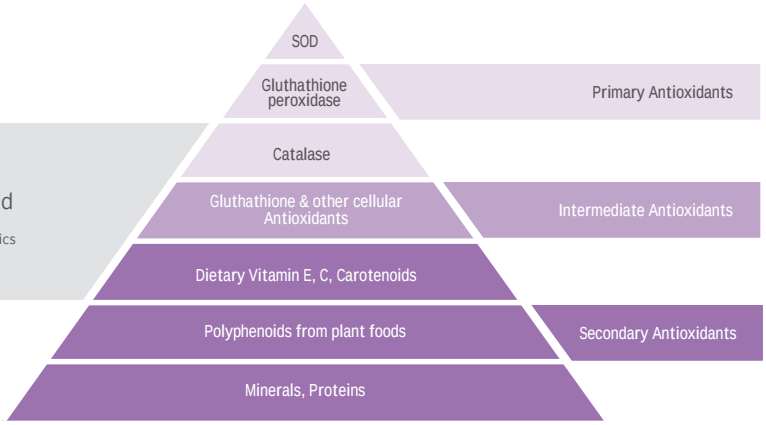

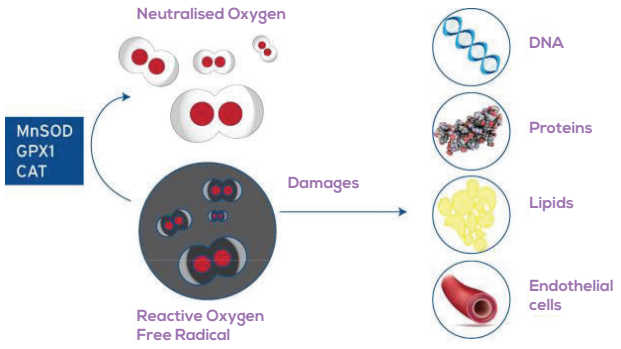

DAMAGE CAUSED BY FREE RADICALS

Excessive amounts of ROS molecules cause oxidative stress that is harmful to cellular metabolism, and may cause unwanted events, such as damage to our DNA, proteins, lipids, the endothelial cells lining our arteries, as well as many other detrimental effects.

The neutralising of ROS in the mitochondria is a 2–step process, with the first step being the conversion of the superoxide ROS to hydrogen peroxide by manganese superoxide dismutase (MnSOD). However, the job is only partly done as hydrogen peroxide is itself an ROS and independently harmful. That is why both a hydrogen peroxide catalase (CAT) and glutathione peroxidase (GPx1) are needed to convert the hydrogen peroxide to harmless hydrogen and water.

THE MAJOR PATHWAY USED BY PRIMARY ANTIOXIDANTS IN QUENCHING SUPEROXIDE

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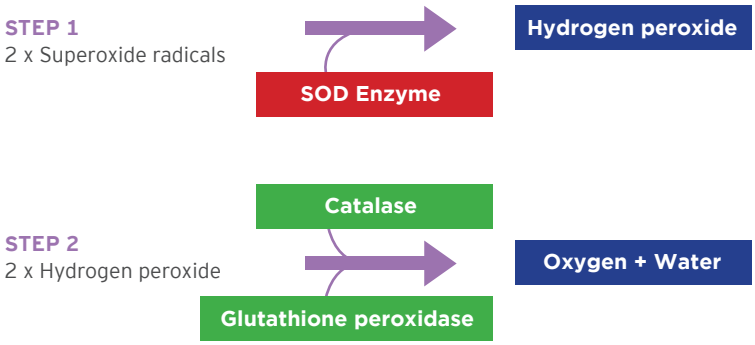


ANTI–OXIDANT STATUS

#	Gene (variant)	Description of the encoded molecule	Your Result			
16	MnSOD (rs4880)	Begins the process of neutralizing ROS. Main enzyme to protect the mitochondria and DNA from oxidative damage. Takes ROS and converts to hydrogen peroxide. Orange dot and particularly red dot indicate decreased production of MnSOD and increased risk of oxidative stress.	T			
17	GPX1 (rs1050450)	Neutralizes hydrogen peroxide by converting to water and oxygen. This enzyme requires glutathione. Orange dot and particularly red dot indicate decreased production of GPx1 and increased risk of oxidative stress.	C			
18	CAT (rs1001179)	Neutralizes hydrogen peroxide by converting to water and oxygen. Orange dot and particularly red dot indicate decreased production of CAT and increased risk of oxidative stress.	A			

DETOXIFICATION AND CELL DEFENCE

Your overall health and wellbeing is not only influenced by the nutrient intake through your diet but also by your body's ability to remove waste products and toxins; substances which are not naturally produced or expected to be present within an organism, or found at higher concentrations than usual. It is essential for all cells to be able to rid themselves of toxins, as they can interfere with cell functions and lead to the development of many diseases. The liver is the primary organ that carries out this detoxification, by rendering toxic substances less harmful and allowing them to be successfully flushed from your body. Other parts of the body that carry out detoxification include the skin, lungs, kidneys and colon.

Substances you ingest through eating, drinking and taking medication lead to toxin accumulation in your body, examples of which include: caffeine, codeine and other opioids, nicotine, alcohol, benzene, polycyclic aromatic hydrocarbons, and heavy metals. Toxins can also come from the environment, such as pollution, passive cigarette smoke, pesticides, or from your own cellular activity. Over–accumulation of toxins can lead to a range of health problems including headaches, muscle and joint pain, fatigue, allergy or flu–like symptoms, inflammation, low exercise tolerance, disturbed sleep, and inability to concentrate.

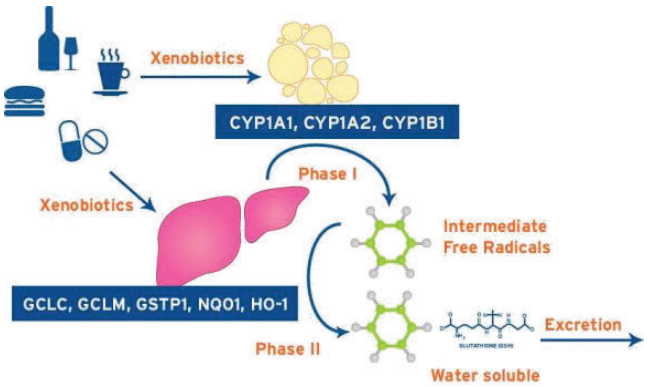
The process of detoxification involves two phases:

1. **Phase I:** performed by phase I enzymes. It is during this stage where toxins become very damaging and a lot of ROS (free radicals) are produced.

2. **Phase II:** performed by phase II enzymes that render these very reactive toxins, safe and enable excretion from your body.

The least beneficial situation, from a detoxification point of view, is to have overactive phase I enzymes and underactive phase II enzymes. In this scenario, you are making lots of very damaging toxins and free radicals (increased oxidative stress) and are unable to render them safe or excrete them.

THE 2 STAGE DETOXIFICATION PROCESS



PHASE I

#	Gene (variant)	Description of the encoded molecule	Your Result			
19	CYP1A1 (rs1048943)	Located mainly in the gut, breast, lungs and skin. Involved in estrogen metabolism. Orange dot and particularly red dot indicate increased enzyme activity and increased levels of reactive toxins and ROS.	A	●		
20	CYP1A2 (rs762551)	Located in the liver, and accounts for 95% of caffeine metabolism. Involved in estrogen metabolism. Red dot indicates decreased CYP1A2 enzyme activity and reduced ability to metabolise caffeine, which can cause health issues with moderate to heavy consumption of caffeine. Orange dot and particularly red dot indicate decreased enzyme activity and slow caffeine clearance. Of note, even for green dot, high caffeine intake can lead to increased levels of reactive toxins and ROS.	CA		●	
21	CYP1B1 (rs1056836)	Located mainly in breast, endometrium and ovaries. Involved in estrogen metabolism. Activity of this enzyme leads to activation of pro-carcinogens. Orange dot and particularly red dot indicate increased enzyme activity and increased levels of reactive toxins and ROS.	C			●

PHASE II

#	Gene (variant)	Description of the encoded molecule	Your Result			
22	GCLC (rs17883901)	First rate limiting enzyme involved in glutathione production. Orange dot and particularly red dot indicate decreased enzyme activity and decreased capacity to produce glutathione for detoxification.	C	●		
23	GCLM (rs41303970)	Second rate limiting enzyme involved in glutathione production. Orange dot and particularly red dot indicate decreased enzyme activity and decreased capacity to produce glutathione for detoxification.	TC		●	
24	GSTP1 (rs1695)	Joins (conjugates) glutathione to toxins, estrogen metabolites and ROS, to render them safe and able to be excreted. Orange dot and particularly red dot indicate decreased enzyme activity and decreased capacity to clear toxins and ROS.	A	●		
25	NQ01 (rs1800566)	Enzyme with strong antioxidant capacity. Described as the anti-cancer enzyme. NQO1 is capable of quenching superoxide and other radical species. Orange dot is extremely reduced enzyme activity and red dot is no enzyme activity.	CT		●	
26	HO-1 (rs2071746)	Enzyme with both anti-inflammatory and anti-oxidant roles. Located mainly in the brain, endothelial cells, gut and lungs. Orange dot and particularly red dot indicate decreased enzyme activity and increased risk of oxidative stress and inflammation.	TA		●	

Genes that affect Vitamin D Metabolism

Research is clearly demonstrating the importance of vitamin D on our health (Hossein–nezhad & Holick, 2013). Unfortunately, vitamin D deficiency affects almost 50% of the world's population (Nair & Maseeh, 2012). Factors contributing to this major health problem include lifestyle factors, such as reduced outdoor activities and obesity, environmental factors, such as living in northern latitudes and air pollution, poor dietary choices, and genetic factors. Recent studies suggest that up to 53% of the human genome contribute to variability in vitamin D levels (Wang et al., 2010).

Vitamin D is found in nearly every cell in the body and exerts its effect on target tissue such as bone, immune, skin, nervous, endothelial, hair follicle, etc, via the vitamin D receptor.

The vitamin D receptor is a protein which binds to vitamin D response elements of vitamin D–responsive genes. If the vitamin D receptor is not functioning well, the body will not benefit from the effect of vitamin D. Research is demonstrating that many of the clinical effects of vitamin D are due to the impact of vitamin D on the inflammatory genes and the immune–regulating role of the pro–inflammatory and anti–inflammatory cytokines.

VITAMIN D RECEPTORS

#	Gene (variant)	Description of the encoded molecule	Your Result			
27	VDR (rs1544410)	Vitamin D receptor, protein that binds to vitamin D. Orange dot and particularly red dot indicate decreased receptor activity and a decreased ability for vitamin D to exert its effect on target tissues such as bone, immune, skin, nervous, endothelial, and hair follicles.	G			
28	VDR-2 (rs731236)		T			

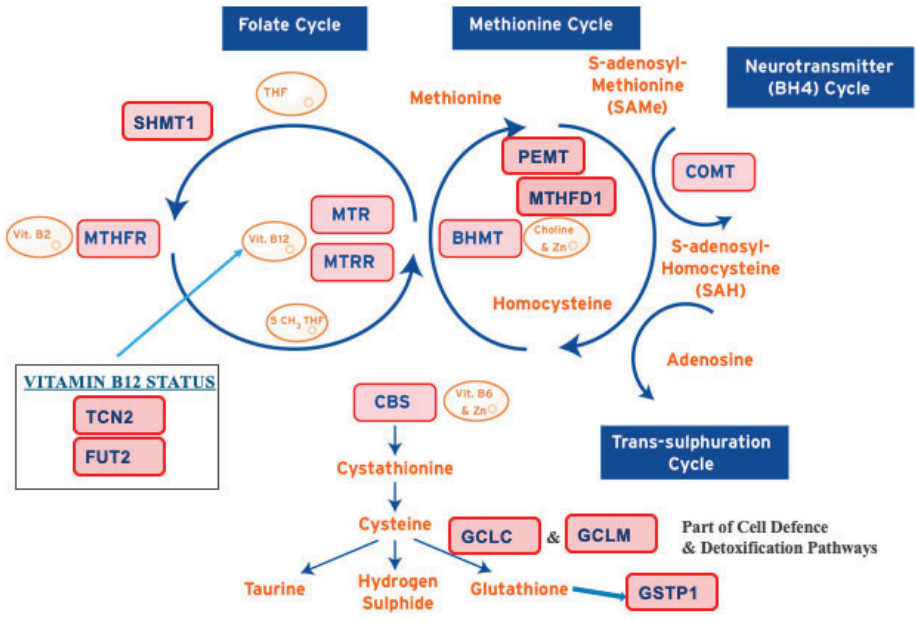
Genes that affect Methylation and Homocysteine Metabolism

Homocysteine is naturally produced within your body as a normal by-product of the breakdown of an essential amino acid called methionine. It is only meant to exist for a brief time before it is converted into other useful substances, such as glutathione and the brain chemicals serotonin (the happy hormone), melatonin (sleep and mood improving hormone), dopamine (euphoria hormone), and adrenaline (the fight and flight hormone). Problems arise, however, when the body accumulates too much of this by-product due to a diet that does not provide the nutrients necessary to metabolise it completely and/or encourages its over-production.

High levels of homocysteine in the blood are believed to increase the chance of heart disease, stroke, diabetes, Alzheimer's disease and osteoporosis to name but a few (Ganguly & Alam, 2015; Huang, Ren, Huang, & Li, 2013; Smith et al., 2018). From a cardiovascular health point of view, high homocysteine levels prevent the normal arterial wall's process of repair, irritate the muscles of the arteries and encourage plaque formation, thus laying the foundation for atherosclerosis, cardiovascular diseases and cerebral vascular disease. High levels of homocysteine can also cause oxidative stress and inflammation.

Some of the main nutrients that help the body breakdown homocysteine are B-vitamins, such as B6, B12, and folic acid. Deficiencies of these nutrients can therefore lead to high homocysteine levels. Vitamin B12 deficiencies are more common in people during mid- to late life. Furthermore, 52% of vegans and 7% of vegetarians can be classified as vitamin B12 deficient (Gilsing et al., 2010). Choline, and essential macronutrient, can also lower homocysteine by participating in its methylation, which is why choline deficiency is also associated with high homocysteine risks. Genetically, some people have a predisposition to poor homocysteine clearance and may require supplementation. Variants in genes involved in the folate, methionine, choline, and trans-sulphuration pathways can influence plasma homocysteine levels.

HOMOCYSTEINE METHYLATION MAP



METHYLATION AND HOMOCYSTEINE METABOLISM

#	Gene (variant)	Description of the encoded molecule	Your Result			
29	MTHFR-1 (rs1801133)	Converts folic acid to the active form of folate, 5-methyltetrahydrofolate. Orange dot and particularly red dot indicate low enzyme activity and decreased levels of the active form of folate.	TC			
30	MTHFR-2 (rs1801131)		CA			
31	MTR (rs1805087)	Donates the methyl group to homocysteine. Orange dot and particularly red dot indicate low enzyme activity which can result in high homocysteine levels.	AG			
32	MTRR (rs1801394)	Keeps the MTR enzyme active. Orange dot and particularly red dot indicate low enzyme activity which can result in high homocysteine levels.	A			
33	PEMT (rs7946)	Choline-metabolising enzyme that modulates the levels of homocysteine. Orange dot and particularly red dot indicate loss of enzyme function, which can alter choline metabolism and lead to high homocysteine levels.	TC			
34	MTHFD1 (rs2236225)	Involved in folate metabolism and choline requirements. Orange dot and particularly red dot indicate higher choline requirements and folate deficiency-associated conditions.	AG			
35	BHMT (rs3733890)	Zn-dependent enzyme, primarily found in the kidneys and liver which uses choline to re-methylate up to 50% homocysteine and therefore has a strong association with circulating homocysteine concentrations. When folate dependent methionine synthesis is impaired, BHMT plays a critical role in homocysteine homeostasis. Orange dot and particularly red dot indicate reduced BHMT activity.	A			
36	SHMT1 (rs1979277)	Cytosolic form of serine hydroxymethyltransferase, which regulates key reactions in folate-mediated one-carbon metabolism. Orange dot and particularly red dot indicate reduced enzyme efficiency and homocysteine accumulation.	A			
37	COMT (rs4680)	Clears noradrenaline, adrenaline, dopamine and catechol estrogen. This enzyme plays an important role in mental health. Over activity and underactivity of this enzyme both have impact on mental health.	G			
38	CBS (rs234706)	Converts homocysteine through to cystathionine to produce hydrogen sulphide, which is a potent vasodilator, and glutathione which is an important anti-oxidant. Green dot particularly and orange dot indicate increased enzyme activity, which is associated with improved health outcomes, such cardiovascular health, compared with the red dot variation.	GA			

VITAMIN B STATUS

Vitamin B12 is an essential micronutrient which is involved in many critical body functions, such as the formation of red blood cells and DNA synthesis during cell division. Clinically, vitamin B12 deficiency is associated with poor health outcomes, such as cardiovascular disease, certain cancers and neurodegenerative disorders. Low vitamin B12 levels are frequently associated with poor intracellular transport of this vitamin or poor intestinal absorption rather than a direct dietary deficiency. Plasma B12 values are inversely related to homocysteine values.

#	Gene (variant)	Description of the encoded molecule	Your Result			
39	TCN2 (rs1801198)	Transcobalamin, carrier protein which binds vitamin B12. Orange and particularly red dot indicate decreased cellular and plasma concentrations of transcobalamin and thereby influence the cellular availability of vitamin B12, resulting in low vitamin B12 status and hence higher homocysteine levels. Of note, this effect is more pronounced in vegetarians and vegans compared with the rest of the population.	C			
40	FUT2 (rs602662)	Implicated in susceptibility to bacterial infections, as it is responsible for the synthesis of the H antigen in body fluids and on the intestinal mucosa, indirectly affecting vitamin B12 levels. Orange dot and particularly red dot indicate lower plasma vitamin B12 levels.	A			

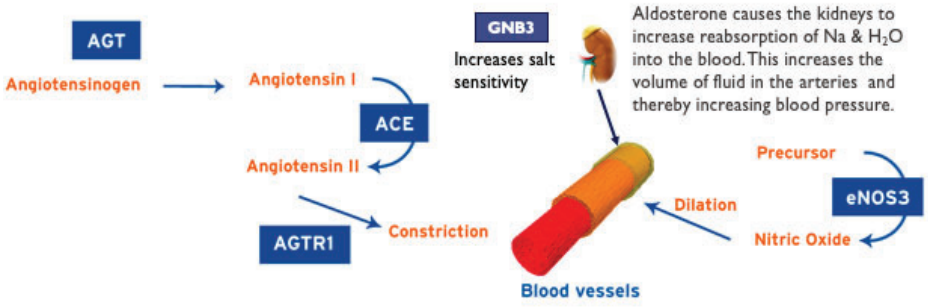
Genes that affect Cardiovascular Health

Cardiovascular disease is the number one cause of death globally. Essentially, your cardiovascular system delivers oxygen and nutrients to every cell in your body and removes carbon dioxide and waste products. Your blood vessels must be healthy and free of disease in order to perform this function well. Blood flow is controlled by Influencing vasoconstriction (narrowing of the blood vessels) and vasodilation (widening the blood vessels). Too much vasoconstriction, and the inability to vasodilate, leads to a narrowing of the blood vessels resulting in high blood pressure. Some people are genetically prone to vasoconstriction and are at risk of being unable to vasodilate effectively.

Blood flow can also be compromised by the build–up of plaque in the blood vessels, or the blood vessels becoming inelastic and stiff. Some people are genetically prone to plaque build–up and their blood vessels becoming stiff and inelastic. Inflammation and oxidative stress will damage your blood vessels and the lining of your blood vessels (endothelium). When the blood vessels and the endothelium are damaged, your blood vessels become stiff and inelastic and prone to plaque build–up. Cardiovascular disease is caused by oxidative stress and inflammation.

High levels of homocysteine in the blood cause oxidative stress and inflammation and increase the risk of atherosclerosis and blood clotting. Genetically, some people are predisposed to poor homocysteine clearance, and therefore it would tend to build up, increasing the risk of cardiovascular disease.

BLOOD PRESSURE REGULATION



- Variations in AGT, ACE and AGTR1 cause increased enzyme activity = High Blood Pressure Risk.
- Variation eNOS3 causes slow enzyme activity = Reduced Blood Volume and reduced VO_2max = Lower aerobic performance.

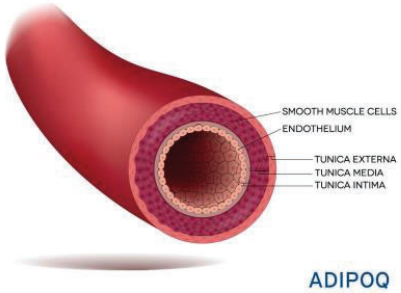
BLOOD PRESSURE REGULATION

#	Gene (variant)	Description of the encoded molecule	Your Result			
41	AGT (rs699)	Angiotensinogen, part of the renin-angiotensin system, which regulates blood pressure and balance of fluids and salts in the body. Orange dot and particularly red dot indicate increased production of angiotensinogen, which can result in increased vasoconstriction and high blood pressure.	CT			
42	ACE (rs4343)	Converts angiotensinogen I to angiotensinogen II, and is also part of the renin-angiotensin system. Orange dot and particularly red dot indicate increased conversion which can result in increased vasoconstriction and high blood pressure. Of note, many blood pressure medications are ACE inhibitors.	D			
43	AGTR1 (rs5186)	Angiotensin II receptor type 1, also part of the renin-angiotensin system. Orange dot and particularly red dot indicate increased receptor function, which can result in increased vasoconstriction and high blood pressure.	A			
44	GNβ3 (rs5443)	Works as a modulator or transducer in various transmembrane signalling systems. Orange dot and particularly red dot indicate increased risk of essential hypertension.	CT			

VASCULAR TONE

eNOS
Synthesis of nitric oxide (NO) in the endothelium (blood vessels) producing vasodilation.

PAI-1
Active in blood vessels. Controls cell adhesion and clotting increases inflammation.



NADPH CYBA
Increases ROS in Endothelial cells causing dysfunction and damage to the blood vessels.

ADIPOQ
An anti-inflammatory cytokine with anti-atherogenic properties.

VASCULAR HEALTH

#	Gene (variant)	Description of the encoded molecule	Your Result			
45	eNOS3-2 (rs1799983)	Involved in nitric oxide production. Orange dot and particularly red dot indicate decreased enzyme activity, which can result in decreased production of nitric oxide and a decreased ability to vasodilate, leading to high blood pressure.	G			
46	NADPH-CYBA (rs4673)	Produces ROS in the endothelial cells. Orange dot and particularly red dot indicate increased enzyme activity which leads to increased oxidative stress and damage to the blood vessels.	C			
47	PAI-1 (rs1799889)	Very active enzyme in your blood vessels. Orange dot and particularly red dot indicate increased enzyme activity which can increase risk of atherosclerosis, atherothrombosis, metabolic syndrome and abnormal blood lipids.	4G/5G			
48	ADIPOQ (rs1501299)	Suppresses pro-inflammatory cytokines, induces anti-inflammatory cytokines and improves response to insulin. Orange dot and particularly red dot indicate decreased production and increased risk of diabetes and atherosclerosis.	C			

Genes that affect Fat Metabolism & Cholesterol Regulation

Maintaining a healthy weight is vital for your health. Obesity is more than unhealthy; it is life threatening. Obesity increases your risk of diabetes, cardiovascular disease, stroke, certain cancers, and joints problems. It also leads to increased inflammation and oxidative stress.

Your lifestyle choices around diet and exercise play a major role in weight maintenance. However, your genes also have a major role in this. Weight maintenance and weight loss is not simply about calories in and calories out. Some people are genetically more prone to having a weight problem. Your genes influence your fat metabolism in a number of ways: how much fat you can tolerate, how much fat you absorb from food, how much body fat you can make, how effectively you can burn body fat, or the best type of exercise for you to burn body fat. In addition, you have genes that influence appetite control and satiety. Some people are genetically prone to overeating, more inclined to want high fat, high carbohydrate food and feeling as if they have not had enough to eat and not feeling satisfied or full.

Understanding these genetic influences enables you to make the best choices around diet and exercise for successful weight loss and long–term weight maintenance.

Fat – Appetite*	Fat Absorption	Fat Storage	Fat Conversion	Fat Metabolism -Energy	Fat Metabolism - Heat	Fat Transport (Cholesterol)
MC4R	FABP2	PPARγ	FADS1	ADRß2	UCP1	CETP
FTO		PPARγC1A		ADRß3	UCP3	LIPC
LEPR1				PPARγC1A		PON1
LEPR2				LEPR-1		PPARδ
				LEPR-2		

*i.e. Preference for fatty foods, carbohydrates, and energy dense foods.

FAT METABOLISM

#	Gene (variant)	Description of the encoded molecule	Your Result			
49	FABP2 (rs1799883)	Fatty-acid binding protein that strongly influences fat absorption. Orange dot and particularly the red dot indicate increased activity and increased fat absorption, resulting in increased risk of obesity, difficulty losing weight, increased leptin and decreased glucose tolerance.	GA			
50	PPARγ (rs1801282)	Regulates fat metabolism, energy storage, insulin sensitivity and glucose control. Orange dot and particularly the red dot indicate decreased binding of this protein to target genes, leading to weight gain, difficulty losing weight, and poor tolerance to dietary fats.	C			
51	PPARγC1A (rs8192678)	Has a critical role in the maintenance of glucose, lipid, and energy homeostasis. Co activator of antioxidant genes and is a master regulator of mitochondrial function and mitochondrial gene expression. Orange dot and particularly the red dot indicate decreased activity of this protein. This can lead to increased risk of obesity, diabetes, neurodegeneration and cardiomyopathy.	G			
52	MC4R (rs12970134)	Membrane-bound receptor for melanocortin 4, key regulator of body weight. Orange dot and particularly red dot indicate decreased appetite and increased daily caloric intake, and therefore higher risk of obesity.	AG			
53	FTO (rs9939609)	Fat mass and obesity-associated gene, known as the "fat gene". Orange dot and particularly red dot indicate higher risk of obesity, owing to increased desire to eat and diminished satiety after meals.	TA			
54	LEPR-1 (rs1137101)	Receptor for leptin, which regulates hunger and satiety, among other complex processes. Orange dot and particularly red dot indicate higher leptin levels, leading to leptin resistance and decreased level of fullness.	GA			
55	LEPR-2 (rs1137100)		AG			
56	FADS1 (rs174537)	Involved in generating long chain polyunsaturated fatty acids from shorter fatty acids. Orange dot and particularly red dot indicate decreased gene function, and therefore higher amounts of "bad fat".	TG			

ENERGY METABOLISM AND THERMOGENESIS

Your body is composed of a variety of different types of tissues, which have different rates of fat metabolism. For example, so called 'lean' tissues, such as muscle, bone and organs, are metabolically very active, whereas adipose tissue (body fat) is not. This fact has important consequences for your overall health, as once the percentage of body fat for men creeps over 25% and for women over 32%, there is a dramatic correlation with illness and disease (Zeng, Dong, Sun, Xie, & Cui, 2012). Hormones, such as adrenaline, noradrenaline, and dopamine, are involved in the breakdown and mobilisation of fat cells for energy in response to stress and exercise, by activating molecules called beta adrenergic receptors.

#	Gene (variant)	Description of the encoded molecule	Your Result			
57	ADRβ2 (rs1042714)	Beta-2 adrenergic receptor. It is involved in energy balance regulation through the stimulation of both thermogenesis (heat production) and fat mobilisation in fat tissue and in breakdown of fats. Orange dot and particularly red dot indicate decreased receptor function and decreased ability to burn body fat.	C			
58	ADRβ3 (rs4994)	Beta-3 adrenergic receptor. It is involved in energy balance regulation by controlling thermogenesis, and fat breakdown and mobilisation in adipose tissue. Orange dot and particularly red dot indicate decreased receptor function and decreased ability to burn body fat.	T			
59	UCP1 (rs1800592)	Uncoupling proteins, which belong to the family of mitochondrial transporter proteins, generating heat rather than energy from the breakdown of fats and leading towards fat loss. Orange dot and particularly red dot indicate decreased activity and decreased ability to burn body fat for heat. Of note, resistance (weights) exercise is the best exercise for fat burning in people who have orange or red dots.	GA			
60	UCP3-2 (rs1800849)		G			

CHOLESTEROL REGULATION

Cholesterol is a lipid produced by all cells. It is an essential structural component of cell membranes and maintains both membrane structural integrity and fluidity. In addition to its importance within your cells, cholesterol also serves as a precursor for the biosynthesis of steroid hormones, bile acids and vitamin D. A number of genes are involved in cholesterol regulation.

#	Gene (variant)	Description of the encoded molecule	Your Result			
61	CETP (rs708272)	Cholesteryl ester transfer protein, manufactured in the liver. It is predominantly bound to HDL in blood and can decrease plasma HDL. Orange dot and particularly red dot indicate increased enzyme activity and increased risk of having low high-density lipoprotein HDL (good) cholesterol.	T			
62	LIPC (rs1800588)	Enzyme expressed in the liver and adrenal glands that breaks down lipids. It assists in transporting high-density lipoproteins which carry cholesterol and triglycerides. Orange dot and particularly red dot indicate increased enzyme activity and increased risk of having low HDL cholesterol.	C			
63	PON-1 (rs662)	Antioxidant protein produced in the liver that protects against LDL oxidation from free radicals by metabolising lipid peroxides and protecting against their accumulation of LDL. Oxidized LDL is a major cardiovascular risk factor. Orange dot and particularly red dot indicate decreased enzyme activity and increased risk of having oxidized low-density lipoprotein (LDL).	AG			
64	PPARδ (rs2016520)	Plays important roles in lipid absorption and intestinal physiology, and it is also involved in cholesterol metabolism. Orange dot and particularly red dot indicate increased risk of having lowered plasma HDL cholesterol and elevated LDL cholesterol levels, especially on a high-fat diet.	TC			

Your Personal Genetic Profile Summary

GENETIC PROFILE ID: 3000041

This report has been designed to identify any of your variants in key genes of major physiological pathways (inflammation, cellular defence, vitamin D metabolism, methylation and homocysteine metabolism, cardiovascular health, and fat metabolism and cholesterol regulation) that may influence the way your body functions, and how it responds to what you eat, how you exercise, and how you live your life, as well as your risk for a number of health issues related to these pathways. The result of your genetic test can lead to three possible outcomes:

Beneficial	Less Beneficial	Least Beneficial
One or both of the alleles in the gene pair contribute to the normal healthy functioning of the gene product.	One of the alleles in the gene pair is contributing to a situation that impairs the healthy functioning of the gene product.	Both of the alleles in the gene pair are contributing to a situation that impairs the healthy functioning of the gene product.

#	Gene	Reported Variant	rsID	Your Result			
INFLAMMATION - Pro-inflammatory Cytokines							
1	IL-1α-1	-889C>T	rs1800587	TC		🟡	
2	IL-1α-2	+4845G>T	rs17561	GT		🟡	
3	IL-1-β	-511G>A	rs16944	G	🟢		
4	IL-6	-174 G>C	rs1800795	C			🔴
5	IL-8	-251T>A	rs4073	TA		🟡	
6	IL-18	-607C>A (G>T)	rs1946518	GT		🟡	
7	TNFα	-308 G>A	rs1800629	GA		🟡	
8	CRP-1	+0169171C>T	rs2794520	TC		🟡	
9	CRP-2	+0143294C>T (G>A)	rs2592887	GA		🟡	
10	CRP-3	3872C>T	rs1205	CT		🟡	
11	COX-2-3	-1195A>G	rs689466	A			🔴
12	COX-2-4	+8473T>C	rs5275	CT		🟡	
INFLAMMATION - Anti-inflammatory Cytokines							
13	IL-10-1	-1082G>A	rs1800896	GA		🟡	
14	IL-10-2	-819C>T	rs1800871	TC		🟡	
15	IL-10-3	-592C>A	rs1800872	CA		🟡	
CELLULAR DEFENCE - Anti-oxidant Status							
16	MnSOD	Val16Ala	rs4880	T	🟢		
17	GPX1	Pro198Leu	rs1050450	C	🟢		
18	CAT	+262T>C (A>G)	rs1001179	A			🔴
CELLULAR DEFENCE - Detoxification and Cell Defence - Phase I							
19	CYP1A1	+ 4889A>G, (Ile462Val)	rs1048943	A	🟢		
20	CYP1A2	-164A>C	rs762551	CA		🟡	
21	CYP1B1	+4326C>G, (Leu432Val)	rs1056836	C			🔴

#	Gene	Reported Variant	rsID	Your Result			
CELLULAR DEFENCE - Detoxification and Cell Defence - Phase II							
22	GCLC	-129C>T	rs17883901	C	🟢		
23	GCLM	-588C>T	rs41303970	TC		🟡	
24	GSTP1	+313A>G, (Ile105V)	rs1695	A	🟢		
25	NQ01	+609 C>T	rs1800566	CT		🟡	
26	HO-1	+413A>T	rs2071746	TA		🟡	
VITAMIN D METABOLISM - Vitamin D Receptors							
27	VDR	BsmI RFLP	rs1544410	G			🔴
28	VDR-2	Taq1 C>T	rs731236	T			🔴
METHYLATION AND HOMOCYSTEINE METABOLISM - Methylation and Homocysteine Metabolism							
29	MTHFR-1	+677 C>T	rs1801133	TC		🟡	
30	MTHFR-2	+1298A>C	rs1801131	CA		🟡	
31	MTR	-2756A>G	rs1805087	AG		🟡	
32	MTRR	-66A>G	rs1801394	A	🟢		
33	PEMT	+5465G>A	rs7946	TC		🟡	
34	MTHFD1	+1958G>A	rs2236225	AG		🟡	
35	BHMT	+742G>A, (Arg239Gln)	rs3733890	A			🔴
36	SHMT1	+1420C>T	rs1979277	A			🔴
37	COMT	Val158Met	rs4680	G	🟢		
38	CBS	+699C>T (G>A)	rs234706	GA		🟡	
METHYLATION AND HOMOCYSTEINE METABOLISM - Vitamin B12 Status							
39	TCN2	+776 C>G (Pro259Arg)	rs1801198	C	🟢		
40	FUT2	A>G(T>C), (Ser258Gly)	rs602662	A	🟢		

#	Gene	Reported Variant	rsID	Your Result			
CARDIOVASCULAR HEALTH - Blood Pressure Regulation							
41	AGT	M235T	rs699	CT		🟡	
42	ACE	Ins. / Del.	rs4343	D			🔴
43	AGTR1	+1166A>C	rs5186	A	🟢		
44	GNβ3	C825T	rs5443	CT		🟡	
CARDIOVASCULAR HEALTH - Vascular Tone							
45	eNOS3-2	+894G>T	rs1799983	G	🟢		
46	NADPH-CYBA	+242C>T	rs4673	C			🔴
47	PAI-1	4G/5G	rs1799889	4G/5 G		🟡	
48	ADIPOQ	+276 G>T (C>A)	rs1501299	C			🔴
FAT METABOLISM & CHOLESTEROL REGULATION - Fat Metabolism							
49	FABP2	Ala54Thr	rs1799883	GA		🟡	
50	PPARγ	Pro12Ala	rs1801282	C	🟢		
51	PPARγC1A	Gly482Ser	rs8192678	G	🟢		
52	MC4R	G>A	rs12970134	AG		🟡	
53	FTO	A>C (T>A)	rs9939609	TA		🟡	
54	LEPR-1	Gln223Arg	rs1137101	GA		🟡	
55	LEPR-2	Lys109Arg	rs1137100	AG		🟡	
56	FADS1	Intron G/T	rs174537	TG		🟡	
FAT METABOLISM & CHOLESTEROL REGULATION - Energy Metabolism and Thermogenesis							
57	ADRβ2	(Gln27Glu)	rs1042714	C	🟢		
58	ADRβ3	(Trp64Arg)	rs4994	T	🟢		
59	UCP1	-3826A>G	rs1800592	GA		🟡	
60	UCP3-2	-55C>T	rs1800849	G			🔴
FAT METABOLISM & CHOLESTEROL REGULATION - Cholesterol Regulation							
61	CETP	+279G>A (C>T)	rs708272	T	🟢		
62	LIPC	-514C>T	rs1800588	C			🔴
63	PON-1	(Q192R)	rs662	AG		🟡	
64	PPARδ	+294T > C	rs2016520	TC		🟡	

ALL GENE-SPECIFIC REFERENCES CAN BE FOUND IN PRACWARE

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