



**dna health**<sup>®</sup>

optimal health for life

## genotype report

Name:

Date of Birth:

Sample Number:

Referring Practitioner:

Date Reported:

## Welcome to your dna health report

From your buccal swab sample we have used a process called the Polymerase Chain Reaction (PCR), which copies the DNA of your genes many times over so that we can generate sufficient quantities to analyse your genetic material. We then identify unique DNA sequences in some of your genes. Certain changes (polymorphisms) in these genes have been studied in detail, with evidence that correlates these polymorphisms with an individual's risk of developing certain chronic disease conditions or altered metabolic processes. Having identified the presence or absence of these polymorphisms, we are able to qualitatively assess particular areas of health risk related to the specific genes. To make a holistic assessment of health risks, environmental factors (diet and lifestyle) need to be considered in conjunction with the accompanying genetic profile.

## How to read your results

You will find your genetic results in the following pages. On the left side you will see the gene name and description. On the right side you will find your specific result and an explanation of the results, associated risks, and diet and lifestyle recommendations. The impact can be identified by the colour of the circle (please see the key below).

No impact:



Mild impact:



Moderate impact:



High impact:



Beneficial impact:



## Lipid metabolism

Heart health depends on a complex balance of environmental, dietary and genetic factors. Certain genes influence LDL and HDL cholesterol levels; higher levels of LDL, or 'bad' cholesterol, and lower levels of HDL or 'good' cholesterol, are associated with a higher risk of heart disease.

Gene Name	Genetic Variation	Your Result	Gene Impact
LPL	1595 C>G	CC	
CETP	279 G>A	AG	
APOC3	3175 C>G	GG	
APOE	E2/E3/E4	E3/E4	

### LPL 1595 C>G

Lipoprotein lipase is anchored to the vascular endothelium and removes lipids from the circulation by hydrolysing triglycerides present in VLDL into free fatty acids. The 1595 C>G variant is a strong indicator of body fat, fat distribution, plasma lipids and insulin concentrations.

YOUR RESULT: **CC**



The analysis identified no genetic variation at the 1595 C>G locus.

### CETP 279 G>A

Cholesterol ester transfer protein plays a key role in the metabolism of HDL and mediates the exchange of lipids between lipoproteins, resulting in the eventual uptake of cholesterol by hepatocytes (reverse cholesterol transport). High plasma CETP concentration is associated with reduced HDL-C concentrations. CETP is a strong and independent risk factor for CAD.

YOUR RESULT: **GA**



The 279 A allele is associated with reduced plasma CETP levels, increased HDL-C levels and reduced risk of cardiovascular disease.

An alpha-linoleic acid-enriched (ALA), low cholesterol diet is effective in decreasing VLDL-C and LDL-C levels in GA and AA individuals.

## Lipid metabolism continued

### APOC3 3175 C>G

Apolipoprotein C3 plays an important role in cholesterol metabolism. It inhibits lipoprotein lipase and hepatic lipase, delaying catabolism of triglyceride-rich particles.

YOUR RESULT: **GG**



The G allele is associated with elevated plasma triacylglycerol, cholesterol, and APOC3 concentrations. Carriers of the G variant have an approximate 4-fold increased risk of hypertriglyceridemia. They are however responsive to dietary intervention. Decrease saturated fat and increase MUFA. If triglycerides are raised, modify CHO intake. Carriers of the G variant may also show enhanced benefit to statin therapy.

### APOE E2/E3/E4

Apolipoprotein E has a multi-functional role in lipoprotein metabolism and is essential for the normal catabolism of triglyceride-rich lipoprotein constituents. Two SNPs result in three allelic isoforms, affecting the protein conformation and thus the receptor binding activity and lipoprotein preference of the APOE protein.

YOUR RESULT: **E3/E4**



The E4 isoform contributes toward a 40 to 50% increased risk of CVD, which is due to higher levels of total- and LDL cholesterol. E4 carriers are hyper-responsive to toxins such as alcohol and smoking, as well as the total fat and fatty acid content of the diet. E4 individuals have a greater anti-oxidant requirement. Reduce the total fat, specifically saturated fat, intake in the diet. Increase anti-oxidant intake and reduce oxidative stress (Decrease alcohol intake, cessation of smoking, weight loss).

## Methylation

B vitamins provide building blocks for growing cells, which are constantly being renewed, and play an important role in many physiological processes. B vitamins also sup ls necessary for protecting our genes, so that our DNA doesn't accumulate damage from the wear and tear in the daily lives of our cells. These vitamins – including folate, vitamins B6 and B12 – help make new DNA for cells that are constantly growing and renewing themselves. Folate is also involved in turning many genes on and off, and also helps repair DNA. The process of DNA repair is called methylation. Although B vitamins are only required in small amounts, they are crucial for methylation and in producing new DNA.

Gene Name	Genetic Variation	Your Result	Gene Impact
MTHFR	677 C>T	CC	
	1298 A>C	CC	
MTR	2576 A>G	AA	
MTRR	66 A>G	AA	
CBS	699 C>T	TT	
COMT	472 G>A	GG	

### MTHFR 677 C>T

Methylenetetrahydrofolate Reductase is a key enzyme in the folate metabolism pathway – directing folate from the diet either to DNA synthesis or homocysteine remethylation.

YOUR RESULT: **CC**



The CC genotype shows normal function.

### MTHFR 1298 A>C

Methylenetetrahydrofolate Reductase is a key enzyme in the folate metabolism pathway – directing folate from the diet either to DNA synthesis or homocysteine remethylation.

YOUR RESULT: **CC**



The C allele is associated with decreased enzyme function. Folate requirements are increased and supplementation of Folate, B2, B6 and B12 may be desirable.

## Methylation continued

### MTR 2576 A>G

Methionine Synthase encodes the enzyme that catalyses the remethylation of homocysteine to methionine.

YOUR RESULT: **AA**



No variation was detected at the 25776 A>G locus.

### MTRR 66 A>G

Methionine Synthase Reductase catalyses methylcobalamin, an essential cofactor of methionine synthase (MTR), which is essential for maintaining adequate intracellular pools of methionine and is also responsible for maintaining homocysteine concentrations at non-toxic levels.

YOUR RESULT: **AA**



No variant was detected at the 66 A>G locus.

### CBS 699 C>T

Cystathionine beta synthase catalyses the conversion of homocysteine to cystathionine and is directly involved in the removal of homocysteine from the methionine cycle, thus any alterations in its activity could affect homocysteine levels.

YOUR RESULT: **TT**



The variant 699T allele is associated with decreased risk of CAD and an increased responsiveness to the homocysteine lowering effects of folic acid. Check dietary folate intake and homocysteine levels and supplement if necessary.

### COMT 472 G>A

Soluble catechol-O-methyltransferase (S-COMT) helps control the levels of certain hormones and is involved in the inactivation of the catecholamine neurotransmitters (dopamine, epinephrine, and norepinephrine). The enzyme introduces a methyl group to the catecholamine, which is donated by S-adenosyl methionine (SAM). Any compound having a catechol structure, like catecholestrogens and catechol-containing flavonoids, are substrates of COMT.

YOUR RESULT: **GG**



No variation was detected at the 472 G>A locus.

## Detoxification

The detoxification process in the body is governed primarily by the GST family of enzymes. Glutathione S-transferases are responsible for catalysing reactions in which the products of Phase I metabolism are conjugated with glutathione, thus making them more water soluble and more easily excreted from the body through sweat and urine. Cruciferous and allium vegetables help increase the activity of your detoxification system, which aids the removal of harmful substances from your body.

Gene Name	Genetic Variation	Your Result	Gene Impact
CYP1A1	Msp1 T>C	TT	
	Ile462Val A>G	AA	
GSTM1	Insertion/Deletion	Deletion	  
GSTP1	313 A>G	GG	 
GSTT1	Insertion / Deletion	Insertion	
NQ01	NQ01 C>T	TC	 

### Phase I Detoxification

#### CYP1A1 Msp1 T>C

The CYP1A1 gene encodes a phase I cytochrome P450 enzyme that converts environmental procarcinogens such as PAHs and aromatic amines to reactive intermediates having carcinogenic effects. In addition, CYP1A1 is involved in the oxidative metabolism of oestrogens, which may play a critical role in the aetiology of breast and prostate cancer.

YOUR RESULT: **TT**



No variation was detected.

#### CYP1A1 Ile462Val A>G

The CYP1A1 gene encodes a phase I cytochrome P-450 enzyme that converts environmental procarcinogens such as PAHs and aromatic amines to reactive intermediates having carcinogenic effects. In addition, CYP1A1 is involved in the oxidative metabolism of oestrogens, which may play a critical role in the aetiology of breast and prostate cancer.

YOUR RESULT: **AA**



No variant was detected.

# Detoxification continued

## Phase II Detoxification

### **GSTM1** Insertion/Deletion

Glutathione S-transferase M1 is the most biologically active member of the GST super-family and is involved in Phase II detoxification in the liver. It is responsible for the removal of xenobiotics, carcinogens, and products of oxidative stress.

### YOUR RESULT: **Deletion**



A deletion results in an absence of the enzyme, leading to reduced capacity for hepatic detoxification and increased risk of various cancers, chemical sensitivity, coronary artery disease in smokers, atopic asthma, and deficits in lung function.

Recommend a diet rich in antioxidants and minimize exposure to toxins. Substantially increase intake of cruciferous and allium vegetables to increase activity of other GST enzymes. When dietary intake is inadequate a high quality supplement containing DIM may be required.

### **GSTP1** 313 A>G

Oxidative stress is a risk factor shared by most disorders implicating GST, and it appears that the efficiency of the GSTP1 enzyme may have an impact on the development and prognosis of diseases influenced by oxidative stress. GSTP1 is the most abundant GST subtype in the lungs and is known to metabolize many carcinogenic compounds.

### YOUR RESULT: **GG**



The G allele decreases activity of the enzyme. Conjugation activity is around 80% for carriers of one G allele, and 70% for the GG genotype individuals.

GST enzyme activities are induced in part by the products of cruciferous and allium vegetables. These should be increased significantly in the diet to increase activity of other GST enzymes to compensate for decreased activity. Daily intake is recommended. When dietary intake is inadequate a high quality supplement containing DIM may be required.

# Detoxification continued

## Phase II Detoxification continued

### **GSTT1** Insertion / Deletion

GSTT1 is a member of a super family of proteins that catalyse the conjugation of reduced glutathione to a variety of electrophilic and hydrophobic compounds.

YOUR RESULT: **Insertion**



No deletion was detected.

### **NQO1** 609 C>T

NADP(H:) quinone oxidoreductase 1 (NQO1) often referred to as Quinone Reductase is primarily involved in the detoxification of potentially mutagenic and carcinogenic quinones derived from tobacco smoke, diet and oestrogen metabolism. NQO1 also protects cells from oxidative stress by maintaining the antioxidant forms of ubiquinone and vitamin E.

YOUR RESULT: **CT**



The variant is a C-to-T transition resulting in a proline to serine amino acid substitution at codon 187 in the protein. The variant T allele results in reduced enzymatic activity. Compared with the wild type CC genotype, the heterozygote variant (CT) has a three-fold decrease in enzyme activity. Individuals with the CT genotype show an increased risk for developing certain cancers including breast, colorectal and gastrointestinal cancers especially when there is exposure to cigarette smoke. The polymorphism has also been linked to benzene toxicity.

## Inflammation

Inflammation is a normal immune response and an essential step in tissue healing. The release of these inflammatory substances is controlled by genes that govern inflammation. However, when these genes are not 'switched off' the inflammatory response continues. An increasing number of common disorders, such as obesity, heart disease, arthritis and inflammatory bowel disease have been associated with chronic low-grade inflammation.

Gene Name	Genetic Variation	Your Result	Gene Impact
IL-6	-174 G>C	CC	
TNFA	-308 G>A	GG	

### IL-6 -174 G>C

Interleukin 6 is a pro-inflammatory cytokine that plays a crucial role in inflammation and regulates expression of CRP. Low-grade chronic inflammation is associated with obesity and visceral fat deposition, insulin resistance, dyslipidaemia and increased risk for cardiovascular disease.

### YOUR RESULT: **CC**



The C allele of this functional SNP has been associated with raised IL-6 and CRP concentrations and has been associated with inflammation, obesity, insulin resistance, dyslipidaemia and raised systolic blood pressure. All of these are pronounced in smokers.

Individuals with the CC genotype should follow a diet to reduce inflammation that includes increasing n-3 fatty acids, decreasing saturated fatty acids, and increasing anti-oxidants. If dietary intake of n-3 fatty acids is inadequate, supplementation may be required. A healthy weight and avoidance of all smoking is also imperative in managing inflammation.

### TNF-A -308 G>A

Tumour necrosis factor- $\alpha$  (TNF $\alpha$ ), a proinflammatory cytokine secreted by both macrophages and adipocytes has been shown to alter whole body glucose homeostasis, and has been implicated in the development of obesity, obesity-related insulin resistance and dyslipidaemia.

### YOUR RESULT: **GG**



No variant was detected at the -308 G>A locus.

## Oxidative stress

Free radicals are a normal by-product of the body's energy-generating biochemical processes. They are highly reactive with other molecules, and can damage DNA, proteins and cellular membranes. Anti-oxidants are free radical scavengers that interact with the free radical to ensure it is no longer a reactive molecule. Anti-oxidants are found naturally in the body in the form of enzymes, but can also be consumed in a wide variety of foods, especially vegetables and fruits, as well as green tea and red wine.

Gene Name	Genetic Variation	Your Result	Gene Impact
eNOS	894 G>T	<b>GG</b>	
MnSOD/SOD2	-28 C>T	<b>TC</b>	

### eNOS 894 G>T

The endothelium-derived nitric oxide (NO) plays a key role in the regulation of vascular tone and peripheral resistance. It also has vasoprotective effects by suppressing platelet aggregation, leukocyte adhesion and smooth muscle cell proliferation.

YOUR RESULT: **GG**



No variant was detected at the 894 G>T locus.

### SOD2 -28 C>T

The SOD2 enzyme destroys the free radicals which are normally produced within cells and which are damaging to biological systems. The enzyme thus has important anti-oxidant activity within the cell, especially within the mitochondria.

YOUR RESULT: **CT**



There is evidence that people without the variant, i.e. those with the C allele, and with a lower consumption of fruits and vegetables, are at increased risk of developing disease, including the risk of developing certain cancers. It is therefore important for individuals with the C allele to ensure adequate anti-oxidant intake. If dietary intake is inadequate supplementation may be required.

## Bone health

Our bones are not a fixed structure. Our cells work continuously to dissolve old bone and create new bone tissue. After the age of 30, both men and women start losing bone mass; the loss is particularly marked in women after menopause. According to latest research both nutrition and genetic factors play an important role in determining bone health.

Gene Name	Genetic Variation	Your Result	Gene Impact
VDR	Fok1 T>C	TC	
	Bsm1 G>A	GA	
	Taq1 C>T	TC	
COL1A1	1546 G>T	GG	

### VDR

Peak bone mass is to a great extent genetically determined. The vitamin D receptor (VDR) gene accounts for around 70% of the entire genetic influence on bone density, playing an important role in calcium homeostasis, bone cell growth and differentiation, and intestinal calcium absorption.

#### **Fok1** YOUR RESULT: **TC**



The T allele has poorer calcium absorption compared to the C allele. The TT genotype has higher bone turnover and increased bone loss and is associated with a lower BMD and osteoporosis in the lumbar spine. Ensure adequate calcium and Vitamin D intake and reduce caffeine to less than 300 mg/d.

#### **Bsm1** YOUR RESULT: **GA**



The A allele is associated with reduced BMD in a dose-dependent manner, and predisposes to osteoporosis, especially when calcium intake is low.

#### **Taq1** YOUR RESULT: **CT**



The CT genotype is not associated with increased bone turnover.

## Bone health continued

### COL1A1 1546 G>T

Type 1 Collagen is the major protein of bone, and is formed from 2 collagen alpha 1- and one collagen alpha 2 chains.

YOUR RESULT: **GG**



The analysis showed no genetic variation at the 1546 G>T locus.

## Insulin sensitivity

Insulin is a hormone that stimulates the uptake of glucose from the diet into the blood. Those with lowered sensitivity to insulin have a limited ability to respond to the hormone's action. The scientific literature suggests that insulin insensitivity or resistance may play an important role in some of the most common disorders – including, obesity, type 2 diabetes, high blood pressure, heart disease and disrupted fat metabolism. role in determining bone health.

Gene Name	Genetic Variation	Your Result	Gene Impact
PPARG	Pro12Ala or C>G	CC	
TCF7L2	rs7903146 C>T	CC	
SLC2A2	Thr110Ile	CC	
FTO	rs9939609 T>A	AT	

### PPARG Pro12Ala or C>G

Peroxisome proliferator-activated receptor gamma is believed to be involved in adipocyte differentiation. It is a transcription factor activated by fatty acids, which has a major role in adipogenesis and expression of adipocyte-specific genes. It is also involved in the regulation of glucose and lipid metabolism and has been identified as the nuclear receptor for the thiazolidinedione class of insulin-sensitizing drugs.

YOUR RESULT: **CC**



The CC genotype is highly sensitive to the type and amount of fat in the diet, with regards susceptibility to obesity and diabetes. An increase in total dietary fat and saturated fat has been associated with increased waist circumference in CC individuals. Attention should be paid to the quality of fat intake, increasing MUFA's in the diet and decreasing SAT FAT. All diet and lifestyle variables that impact insulin sensitivity should be addressed.

### TCF7L2 rs7903146 C>T

Transcription factor 7-like 2 (TCFL2) gene encodes a transcription factor that regulates blood glucose homeostasis. This SNP influences both insulin secretion and resistance and has been associated with an increased risk of insulin resistance and type 2 diabetes mellitus.

YOUR RESULT: **CC**



No variant was detected.

## Insulin sensitivity continued

### SLC2A2 Thr110Ile

GLUT2, coded by the SLC2a2 gene, facilitates the first step in glucose induced insulin secretion, with the entry of glucose into the pancreatic  $\beta$ cell. Because of its low affinity for glucose, it has been suggested as a glucose sensor, and is considered to be important in the postprandial state, and is involved in food intake and regulation.

YOUR RESULT: **CC**



The analysis detected no variant.

### FTO rs9939609 T>A

Fat-mass-and-obesity-associated (FTO) gene is present at high levels in several metabolically active tissues, including, heart, kidney, and adipose tissue, and is most highly expressed in the brain, particularly in the hypothalamus which is concerned with the regulation of arousal, appetite, temperature, autonomic function, and endocrine systems. It has been suggested that the FTO gene plays a role in appetite regulation and that it is associated with energy expenditure, energy intake, and diminished satiety.

YOUR RESULT: **TA**



The A allele has been associated with higher BMI, body fat percentage and waist circumference, especially in individuals with a sedentary lifestyle. Overweight individuals with the A allele are at increased risk for insulin resistance and diabetes, especially when there is a high fat intake. Modify the diet to include a moderate amount of carbohydrate, increase MUFA and decrease SAT FAT and manage the overall fat intake. Regular physical activity is recommended.

## Food responsiveness

Particular nutrients and certain food components in different foodstuffs can affect individuals in different ways. With new research coming to light in this area, specific genes can be tested to give more insight to how an individual might respond to a particular food component. The areas of food responsiveness covered in this panel include: Lactose intolerance, Polyunsaturated Fat (PUFA) metabolism, caffeine sensitivity, salt sensitivity and iron overload.

	Gene Name	Genetic Variation	Your Result	Gene Impact
Iron overload	HFE	C282Y & H63D	<b>282CC / 63HH</b>	
Lactose intolerance	MCM6	-13910C>T	TC	
Caffeine sensitivity	CYP1A2	A>C	CA	
PUFA metabolism	FADS1	rs174537 G>T	GT	
Salt sensitivity	ACE	I/D	II	
Salt sensitivity	AGT	T>C	TT	

### Iron overload

#### HFE C282Y & H63D

Hereditary hemochromatosis is a genetic disorder in which there is excessive accumulation of iron in the body, leading to iron overload. In individuals with the disorder, the daily absorption of iron from the intestines is greater than the amount needed to replace losses. Since the normal body cannot increase iron excretion, the absorbed iron accumulates in the body. Individuals who carry the genes for hereditary hemochromatosis may have no symptoms or signs and the disease is treatable if detected early. Severe symptoms and signs of iron overload include sexual dysfunction, heart failure, joint pains, liver cirrhosis, diabetes mellitus, fatigue, and hypermelanotic pigmentation.

#### YOUR RESULT: **282CC & 63HH**



The analysis detected no genetic variation increasing risk for the disorder.

## Lactose intolerance

### MCM6 –13910C>T

Adult lactase deficiency is a common condition with a decrease in the ability of the epithelial cells in the small intestine to digest lactose, owing to a physiological decline in the lactase enzyme. After ingestion of milk or other dairy products, individuals who suffer from this condition may experience abdominal cramps, bloating, distension, flatulence and diarrhoea.

### YOUR RESULT: **CT**



The CT genotype is associated with lactase persistence in the caucasian population.

## Caffeine sensitivity

### CYP1A2 A>C

Coffee is a major source of caffeine, which is metabolized by the polymorphic cytochrome P450 1A2 (CYP1A2) enzyme.

### YOUR RESULT: **AC**



Individuals with the CC genotype are associated with a reduced ability to metabolise caffeine. A moderate to high intake of caffeinated beverages, such as coffee, is associated with increased risk of heart disease. It is recommended that these individuals opt for decaffeinated options.

## PUFA metabolism

### FADS1 rs174537 G>T

The delta 5 and delta 6 desaturases, encoded by FADS1 and FADS2 genes, are key enzymes in polyunsaturated fatty acid (PUFA) metabolism that catalyze the conversion of linoleic acid (LA) into arachidonic acid (AA) and that of alpha-linolenic acid (ALA) into eicosapentaenoic acid (EPA). SNPs in the FADS locus have been associated with blood concentrations of long-chain PUFAs as well as with cholesterol concentrations. Based on genetic variation, individuals may require different amounts of dietary PUFAs or LC-PUFAs to achieve comparable biological effects.

### YOUR RESULT: **GT**



The G allele is associated with enhanced conversion of DGLA to AA due to increased enzymatic efficiency and thus appears to be associated with higher levels of AA, systemic inflammation and inflammatory disorders.

## Salt sensitivity

### ACE I/D

ACE codes for the angiotensin-converting enzyme and is part of the renin-angiotensin system, which controls blood pressure by regulating the volume of fluids in the body.

YOUR RESULT: **II**



Studies show that patients with essential hypertension homozygous for the insertion allele of the ACE gene had a significantly higher blood pressure increase with high salt intake compared to DD individuals.

### AGT T>C

Angiotensinogen is expressed in tissues involved in blood pressure regulation such as the kidneys, adrenals and brain. Increased angiotensinogen levels correlate with increased blood pressure. The gene also influences salt sensitivity of blood pressure.

YOUR RESULT: **TT**



No variant was detected.

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