

GENOTYPE REPORT

Patient 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).

EXAMPLE RESULT:

GENE NAME & DESCRIPTION	YOUR RESULT & EXPLANATION
GENE NAME Genetic Variation A brief description of the gene.	YOUR RESULT:  GENE IMPACT COLOUR KEY A brief explanation of the diet, nutrition and lifestyle factors relevant to the particular gene variant being identified.

GENE IMPACT COLOUR KEY:



BENEFICIAL



LOW/NO
IMPACT



MEDIUM
IMPACT



HIGH
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.

LPL

Genetic Variation: 1595 C>G or Ser447Stop

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

Genetic Variation: 279 G>A

Cholesterol esther 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 (ALA) -enriched, low cholesterol diet is effective in decreasing VLDL-C and LDL-C levels in GA and AA individuals.

APOC3

Genetic Variation: 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:

**CC**

The analysis identified no genetic variation at the 3175 C>G locus.

APOE

Genetic Variation: E4 (112Arg/158Arg)

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).

B VITAMINS / 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 supply some of the chemicals 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.

MTHFR

(Genetic Variation: 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

(Genetic Variation: 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:



AA

No genetic variation was detected at the 1298 A>C locus.

MTR

Genetic Variation: 2756 A>G)

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

YOUR
RESULT:



AG

The G allele is associated with decreased levels of homocysteine – the SNP increases activity of the MTR enzyme that converts homocysteine to methionine.

COMT

(Genetic Variation: 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:



GA

The A allele is associated with a 3-4 fold reduction in the methylation activity of the COMT enzyme and is associated with increased risk for breast cancer. Key interventions for beneficial modulation of oestrogen metabolism can be accomplished by increasing insoluble fibre, managing the quality of dietary fat intake, losing weight, and increasing exercise. In addition, ensure sufficient anti-oxidant and magnesium intake. Dietary Components that inhibit COMT activity include quercetin and tea catechins.

B VITAMINS / METHYLATION (continued)

MTRR

(Genetic Variation: 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:**



The G allele is associated with increased risk for premature CAD when cobalamin (Vitamin B12) status is low. Ensure adequate intake of folate, vitamin B12 and vitamin B6.

CBS

(Genetic Variation: 699 C>T)

Cystathionine beta synthase catalyses the conversion of homocysteine to cystathione 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:**



The variant 699T allele is associated with decreased risk of CAD and an increased responsiveness to the homocysteine lowering effects of folic acid. However, in some individuals the upregulated enzyme may have relevance downstream in the methylation pathway.

Check dietary folate intake and homocysteine levels and supplement if necessary.

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.

GSTM1

(Genetic Variation: 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:

 **PRESENT**

No deletion was detected.

GSTP1

(Genetic Variation: 313 A>G or 105 Ile > Val)

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:

 **AA**

The analysis identified no genetic variation at the 313 A>G locus.

GSTT1

(Genetic Variation: 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:

 **ABSENT**

The deletion is associated with an increased risk of lung, larynx and bladder cancers, as well as skin basal carcinomas.

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 or indole 3 carbinol may be required.

DETOXIFICATION (continued)

CYP1A1

(Genetic Variation: 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:



No variant was detected.

CYP1A1

(Genetic Variation: Ile462Val (G>A))

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:



A G to A substitution leads to an amino acid substitution (ile to val) of its protein. The association between this SNP and cancer has been well documented.

The AA genotype is associated with increased enzyme activity resulting in increased rates of carcinogen activation and subsequently DNA damage. In the presence of the A allele it is important to reduce exposure to all diet and environmental procarcinogens such as PAH, aromatic amines, nitrates, and smoking of any kind. In addition attention should be paid to optimising phase 2 detoxification.

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.

IL-6

(Genetic Variation: -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:



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 C allele should follow a diet to reduce inflammation that includes increasing ω -3 fatty acids, decreasing saturated fatty acids, and increasing antioxidants. A healthy weight and avoidance of all smoking is also imperative in managing inflammation.

TNF-A

(Genetic Variation: -308 G>A)

Tumour necrosis factor- α (TNF α), 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:



The A allele results in a two-fold increase in TNFA transcription, which leads to elevated levels of the circulating TNF α protein. The A allele is also associated with increased risk for obesity, adiposity, dyslipidaemia and insulin resistance, especially when dietary fat intake is high. In the presence of the A allele, increase intake of n-3 fatty acids and reduce pro-inflammatory saturated fatty acids. If dietary intake of ω -3 fatty acids is inadequate, supplementation may be required. Weight management is also imperative in managing inflammation.

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.

eNOS

(Genetic Variation: 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:



GT

The T allele affects proteolytic cleavage of the enzyme thereby reducing nitric oxide bio-availability in the blood vessel wall and promoting atherosclerosis, as a result it is associated with atherosclerosis, essential hypertension, end-stage renal disease and pre-eclampsia.

Ensure adequate anti-oxidant and ω -3 fatty acids intake.

MnSOD/SOD2

(Genetic Variation: -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.

SOD3

Genetic Variation: 760 C>G or Arg231Gly

Extracellular superoxide dismutase is the extra-cellular form of superoxide dismutase, and the major antioxidant enzyme system of the vessel wall.

YOUR RESULT:



CG

The SNP results in the accelerated release of the enzyme from the tissue into the plasma, resulting in significantly reduced tissue SOD3 activity. The G allele is associated with increased risk for CAD. There is also evidence that the effect of the G allele is greatly exacerbated by smoking and is associated with lung function. Ensure adequate fruit and vegetable and anti-oxidant intake, and reduce sources of oxidative stress such as smoking.

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.

VDR

(Genetic Variation: Fok1 T>C)

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.

YOUR RESULT:

**CC**

The CC genotype is associated normal calcium absorption.

VDR

(Genetic Variation: Bsm1 C>T (G>A))

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.

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.

VDR

(Genetic Variation: Taq1 C>T)

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.

YOUR RESULT:

**TT**

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.

The TT genotype is associated with normal bone turnover.

COL1A1

(Genetic Variation: 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.

PPARG

(Genetic Variation: Pro12Ala 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

(Genetic Variation: rs7903146 C>T)

Transcription factor 7-like 2 (TCF7L2) 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:



TT

Individuals with the TT genotype have an increased risk for insulin resistance and type 2 diabetes, especially in obese individuals and those with low HDL-C. The T allele has also been associated with less weight loss in response to diet and lifestyle intervention, especially when fat intake is high. Individuals with the TT genotype require diet and lifestyle changes that impact insulin sensitivity.

FTO

(Genetic Variation: 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:



AA

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.

IRON OVERLOAD

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.

HFE

(Genetic Variation: 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 & 63DD

The 63DD genotype can lead to a mild form of the disease. An individual's iron processing deficiency may not reach the level of formally being diagnosed as Hemochromatosis. If diagnosed, Hemochromatosis can be easily treated by phlebotomy or regular donation of blood to reduce blood iron levels. A low-iron diet can also help control accumulation of iron. Those affected should avoid vitamin supplements containing iron and also heavy vitamin C and alcohol consumption which can interfere with iron processing.

Head Office:

Nygade 6, 3.sal • 1164 Copenhagen K • Denmark
+45 33 75 10 00

South Africa Office:

North Block • Thrupps Centre • 204 Oxford Rd • Illove 2196 • South Africa
+27 (0) 11 268 0268

UK Office:

11 Old Factory Buildings • Battenhurst Road • Stonegate • E. Sussex TN5 7DU • UK
+44 (0) 1580 201 687