dna health

PATIENT GENOTYPE REPORT - ***STRICTLY CONFIDENTIAL***

Patient Name:

Date of Birth:

Sample Number:

Date Reported:

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BACKGROUND TO THE ANALYSIS

We received your swab sample and used special molecular techniques to amplify your DNA for further analysis. This process, called the Polymerase Chain Reaction (PCR), 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, and evidence has emerged that correlates these polymorphisms with an individual's risk of developing certain chronic disease conditions or altering metabolic processes. Having identified the presence or absence of these polymorphisms, we are able, qualitatively, to assess particular health risks related to the specific genes. To make a holistic assessment of disease risks, environmental factors (diet and lifestyle) need to be considered in conjunction with the accompanying genetic profile.

In the following pages you will find a table of your genetic results, and an explanation of these results and associated risk including diet and lifestyle recommendations. To highlight that a medium or high impact gene variant has been identified, we use the following symbol alongside the explanation of the genes ⚠

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 RESULTS	GENE IMPACT
LPL	1595 C>G	CC Wildtype	No Impact
CETP	279 G>A	GA Heterozygote	
APOA1	-75 G>A	GG Wildtype	
APOC3	3175 C>G	GC Heterozygote	
APOE	158 Arg>Cys / 112 Cys>Arg	E3/E3 Wildtype	No Impact

 Low Impact

 Medium Impact

 High Impact

GENE EXPLANATIONS

LPL

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. In individuals who carry the G allele, plasma VLDL-C and triglyceride levels are lower and HDL-C levels higher, compared to individuals carrying the C allele.
CC individuals should modify intake of total saturated fat.

APOA1 

Apolipoprotein A1 is the main protein in HDL-C & regulates production of HDL-C.
In individuals with the GG genotype, higher dietary PUFA intake is associated with lower HDL-C levels. Keep PUFA intake at 4% or less of total daily energy intake.
In GA and AA individuals, a higher PUFA intake is associated with higher HDL-C levels. Aim for an intake of PUFA at 8% or greater of total daily energy intake. Maximise the n-3 component of the total PUFA intake.

CETP

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. High plasma CETP concentration is associated with reduced HDL-C concentrations. CETP is a strong and independent risk factor for CAD.

The G allele is associated with increased plasma CETP, lower HDL-C and increased CVD risk. GG genotype responds well to statin therapy.

APOC3

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

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, but are 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/E4, E3/E4, E4/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.

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).

In general, E2 carriers have lower total cholesterol levels. There is some suggestion that the APOE E2 allele may have a slight protective effect against CVD, however, despite lower cholesterol levels, E2 carriers are not immune to dyslipidaemia and raised triglycerides. E2 carriers appear to respond less to dietary intervention, but appear to be more responsive to statin therapy.

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.

GENE NAME	GENETIC VARIATION	YOUR RESULTS	GENE IMPACT
MTHFR	677 C>T	CT Heterozygote	
	1298 A>C	AC Heterozygote	
MTR	2756 A>G	AG Heterozygote	Beneficial
MTRR	66 A>G	AG Heterozygote	
CBS	699 C>T	CT Heterozygote	Beneficial

 Low Impact

 Medium Impact

 High Impact

GENE EXPLANATIONS

MTHFR

Methylenetetrahyrdofolate Reductase is a key enzyme in the folate metabolism pathway – directing folate from the diet either to DNA synthesis or homocysteine remethylation. The T allele lowers activity of the MTHFR enzyme, which results in an increase in homocysteine levels, a decrease in DNA methylation and thus an increase in DNA adducts.

677 C>T 

T allele carriers have increased folate, vitamin B2, B6 & B12 requirements. – Enzyme function is only 70% of optimal in CT individuals and 40% of optimal in TT individuals. In addition to folate-rich foods, a supplement may be recommended. In TT individuals as much as 800ug folate may be required.

1298 A>C

Folate requirements are increased and supplementation of folate, B2, B6 & B12 may be desirable for C allele carriers.

MTR

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

MTRR

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.

The G allele is associated with increased risk for premature CAD and the GG genotype is a significant risk factor for the development of premature CAD and Neural Tube Defects (NTDs) when cobalamin (Vitamin B12) status is low. Ensure adequate intake of folate, vitamin B12 and vitamin B6.

CBS

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.

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.

DETOXIFICATION

The detoxification process in the body is governed primarily by the GST family of enzymes. Glutathione S-tranferases 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 RESULTS	GENE IMPACT
GSTM1	Present/Absent	Present	No Impact
GSTP1	313 A>G	AG Heterozygote	
GSTT1	Present/Absent	Deletion	
CYP1A1	Msp1 T>C	TT Wildtype	No Impact

 Low Impact

 Medium Impact

 High Impact

GENE EXPLANATIONS

GSTM1

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.

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 or indole 3 carbinol may be required.

GSTP1

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.

The G allele decreases activity of the enzyme. Conjugation activity is 82% 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 of these vegetables is recommended. When dietary intake is inadequate a high quality supplement containing DIM or indole 3 carbinol may be required.

GSTT1 

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. 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.

CYP1A1

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.

The variant allele C is associated with increased enzyme activity resulting in elevated levels of activated metabolites and subsequently DNA damage. In the presence of the C 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.

GENE NAME	GENETIC VARIATION	YOUR RESULTS	GENE IMPACT
IL-6	-174 G>Ct	GG Wildtype	No Impact
TNFA	-308 G>A	GA Heterozygote	

 Low Impact

 Medium Impact

 High Impact

GENE EXPLANATIONS

IL-6

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.

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 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.

TNFA 

Tumor necrosis factor-α (TNFα), a proinflammatory cytokine, has been shown to alter whole body glucose homeostasis, and has been implicated in the development of obesity, obesity-related insulin resistance and dyslipidaemia.
The A allele results in a two-fold increase in TNFA transcription, which leads to elevated levels of the circulating TNFα 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 n-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.

GENE NAME	GENETIC VARIATION	YOUR RESULTS	GENE IMPACT
eNOS	894 G>T	GG Wildtype	No Impact
SOD2	16 A>V	TC Heterozygote	
SOD3	760 C>G	CC Wildtype	No Impact

 Low Impact

 Medium Impact

 High Impact

GENE EXPLANATIONS

eNOS

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.

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 n-3 fatty acids intake.

SOD2 

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.

There is evidence that people 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

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

GENE NAME	GENETIC VARIATION	YOUR RESULTS	GENE IMPACT
VDR	Fok1	TC Heterozygote	
	Bsm1	AG Heterozygote	
	Taq1	CT Heterozygote	
COL1A1	1546 G>T	GT Heterozygote	

 Low Impact

 Medium Impact

 High Impact

GENE EXPLANATIONS

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

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. In these individuals ensure adequate calcium and Vitamin D intake and reduce caffeine to less than 300 mg/d. It may be prudent to test Vitamin D levels.

Bsm1

The A allele is associated with reduced BMD in a dose-dependent manner, and predisposes to osteoporosis, especially when calcium intake is low. There is also lower phosphorus re-absorption in the AA genotype when calcium is low in the diet, which results in lower calcium absorption and higher rates of hip fracture. Women with the AA genotype have a high bone loss when their caffeine intake is more than 300mg/day. In these individuals ensure adequate calcium and Vitamin D intake and reduce caffeine to less than 300 mg/d. It may be prudent to test Vitamin D levels.

Taq1

Individuals with the CC genotype have higher bone turnover, increased bone loss and a higher risk of suffering osteoarthritis, which is highest when there is a low calcium intake. Individuals with the CC genotype have higher bone loss when caffeine intake is > 300 mg/d. In these individuals ensure adequate calcium and Vitamin D intake and reduce caffeine to less than 300 mg/d. It may be prudent to test Vitamin D levels.

COL1A1 

Type 1 Collagen is the major protein of bone, and is formed from 2 collagen alpha 1- and one collagen alpha 2 chains. The COL1A1 T allele influences the ratio of collagen alpha chains produced by bone cells, leading to abnormal mineralization of bone and reduced bone strength.

Women with the TT genotype are at significantly increased risk of excess rates of bone loss at the spine. This effect may be nullified by the use of HRT. Individuals with the T allele have increased risk of fracture and greater bone loss when calcium is low. Ensure adequate calcium intake.

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.

GENE NAME	GENETIC VARIATION	YOUR RESULTS	GENE IMPACT
PPAR-y	Pro12Ala	GG Homozygote	Beneficial
FTO	rs9939609 T>A	AA Homozygote	
TCF7L2	rs7903146 C>T	CT Heterozygote	

 Low Impact

 Medium Impact

 High Impact

GENE EXPLANATIONS

PPARG

CC

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.

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.

GG & GC

The G allele is associated with reduced promoter activation, reduced transcriptional activity and reduced adipocyte differentiation. As a result the G allele has been associated with lower BMI and fasting insulin, improved insulin sensitivity and reduced risk of insulin resistance and diabetes

FTO

Fat-mass-and-obesity-associated 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.

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.

TCF7L2

Transcription factor 7-like 2 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.

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.