CLINICAL SERVICES

Practitioner report

FOR PROFESSIONAL REFERENCE ONLY

BioCeuticals

Wellbeing Bundle Report
How to read this report

SNP	A single nucleotide polymorphism is a DNA sequence variation occurring when a single nucleotide adenine (A), thymine (T), cytosine (C) or guanine (G) in the genome differs between paired chromosomes in an individual.
rs number	The rs number is an accession number used by researchers and databases to refer to a specific SNP. It stands for reference SNP cluster ID.
Gene Variation	A variation within a gene such as a SNP
No effect	This result is likely to be associated with normal protein function.
Pay attention	This result may have some effect on protein function. Altered protein function may effect health outcomes.
Pay close attention	This result is likely to have an effect on the protein function. Altered protein function may effect health outcomes.
- -	This is considered the 'wild type' allele. No variant has been inherited.
- +	Heterozygous allele, being inherited from one parent.
+ +	Homozygous allele, being inherited from both parents.

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Research

The gene and SNP results indicated in this report utilise a rating scale to provide an indication of the quality of the research. The evidence is based on Oxford Centre for Evidence Based Medicine (Level of Evidence March 2009) and has been modified by BioCeuticals to apply to genetic tests.

Evidence Rating System

Level	Causation and treatment
5 stars ★★★★★	Systematic review of multiple randomised controller trials (meta-analysis) Systematic review of meta-analyses Single randomised controlled trial with narrow confidence intervals
4 stars ★★★★	Meta-analysis of cohort studies Prospective cohort study with 80% follow-up Single RCT (not supported by at least 5 studies) Good quality ecological research Genome-wide association studies
3 stars ★★★	Multiple-case control studies Meta-analysis of case control Follow up cohort study < 80% Cross-sectional studies (n>1000 subjects; subjects can be additive from multiple studies if direction is the same) Case control (n>100 subjects; more than 1 study in same direction) Multiple studies on human enzyme function/activity
2 stars ★★	Single-case control study (or in multiple studies conflicting in at least three) Cross-sectional study (n<1000 subjects) Case series Single study on human enzyme function/activity
1 star ★	Single-case report Expert opinion Biochemistry First principle Animal/bacteria analogy

Wellbeing Bundle Report

This report covers the full suite of genetic variations (SNPs) available across all BioCeuticals DNA testing profiles.

Genetic variations (SNPs) included relate to mood and cognition, methylation, detoxification and antioxidant enzymes, hormone balance and function, along with nutrient absorption, transport and metabolism.

Legend

- No effect
- Pay attention
- Pay close attention

- - Wild type
- \+ Heterozygous
- \+ \+ Homozygous

Vitamin A metabolism

Gene	Gene variation	rs number	Result	Effect
BCMO1	C1136T	rs7501331	CC - -	

Vitamin B12 absorption and transport

Gene	Gene variation	rs number	Result	Effect
FUT2	G428A	rs601338	GA - +	
FUT2	G772A	rs602662	GA - +	
TCN2	C776G	rs1801198	GG + +	

Vitamin C transport

Gene	Gene variation	rs number	Result	Effect
SLC23A1	G790A	rs33972313	GG - -	

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Legend

- No effect
- Pay attention
- Pay close attention

- - Wild type
- + Heterozygous
+ + Homozygous

Vitamin D

Gene	Gene variation	rs number	Result	Effect
DHCR7	G>T	rs12785878	TT + +	
CYP2R1	G>A	rs10741657	GG + +	
CYP27B1		rs4646536	TT + +	
GC	A>C	rs2282679	CA - +	
VDR	FOK	rs2228570	TC - +	
CYP24A1	T>A	rs6013897	AA + +	

Folate pathway

Gene	Gene variation	rs number	Result	Effect
MTHFD1	G1958A	rs2236225	AA + +	
MTHFD1	C105T	rs1076991	TT + +	
SHMT1	C1420T	rs1979277	CT - +	
MTHFR	C677T	rs1801133	CT - +	
MTHFR	A1298C	rs1801131	AA - -	

Homocysteine-Methionine pathway

Gene	Gene variation	rs number	Result	Effect
MTR	A2756G	rs1805087	AA - -	
MTRR	A66G	rs1801394	AA - -	
BHMT	G742A	rs3733890	GG - -	

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Legend

- No effect
- Pay attention
- Pay close attention
- - Wild type
- - + Heterozygous
- + + Homozygous

Transsulfuration pathway

Gene	Gene variation	rs number	Result	Effect
CBS	C699T	rs234706	CC - -	

Fatty acid related genes

Gene	Gene variation	rs number	Result	Effect
PEMT	G>A	rs7946	GA - +	
FADS1	C53T	rs174546	CT - +	

Phase 1 detox-related genes

Gene	Gene variation	rs number	Result	Effect
CYP17A1	T-34C	rs743572	AG - +	
CYP19A1	C19T	rs10046	CC - -	
CYP1A1	A2455G	rs1048943	AA - -	
CYP1A1/1A2		rs2472297	CT - +	
CYP2A6	A>T	rs1801272	AA - -	
CYP1B1	A10106G	rs1800440	AA - -	
CYP1B1	C1294G/V432L	rs1056836	CG - +	
CYP2D6	*10 *4	rs1065852 rs3892097	*1/*1 - -	
CYP2C19	*17	rs12248560	*1/*1 - -	
CYP3A4*1B	-392A>G	rs2740574	AA - -	

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Legend

- No effect
- Pay attention
- Pay close attention

- - Wild type
- + Heterozygous
+ + Homozygous

Phase 2 detox-related genes

Gene	Gene variation	rs number	Result	Effect
NAT2	Paired SNP T>C Paired SNP C>T	rs1801280 rs1041983	RS - +	
NAT2	Tag SNP G>A	rs1495741	GA - +	
GSTP1	A313G	rs1695	AA - -	
GSTP1	C341T	rs1138272	CC - -	
NQO1	C609T	rs1800566	CT - +	
COMT	G158A	rs4680	GA - +	

Antioxidants

Gene	Gene variation	rs number	Result	Effect
SOD2	C47T	rs4880	CC - -	
GPX1	linkage with rs1050450	rs1800668	CC - -	
CAT	C-262T	rs1001179	CT - +	
PON1	Q192R	rs662	AG - +	

Neurotransmitters and mood

Gene	Gene variation	rs number	Result	Effect
MAO-A	X-chr	rs909525	AA - -	
DRD2/ANNK1	Taq1a	rs1800497	CC - -	
TH	C824T	rs10770141	CT - +	
DAO	C47T	rs10156191	CT - +	
GAD1	147G>A	rs3749034	GG - -	
BDNF	Val66Met	rs6265	GG - -	

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Blood pressure

Gene	Gene variation	rs number	Result		Effect
AGT	T803C	rs699	TT	- -	
NOS3	G894T	rs1799983	GT	- +	

Clotting factors

Gene	Gene variation	rs number	Result		Effect
F2	G20210A	rs1799963	GG	- -	
F5	G1601A	rs6025	GG	- -	

Hormone receptor and thyroid

Gene	Gene variation	rs number	Result		Effect
LHCGR	A226096G	rs13405728	AA	- -	
PGR		rs1042838	GT	- +	
FOXE1	57kb upstream G>A	rs965513	GG	- -	

Legend

- No effect
- Pay attention
- Pay close attention

- - Wild type
- - + Heterozygous
- + + Homozygous

Vitamin A Metabolism > BCMO1

Gene	Gene variation	rs number	Result		Effect
BCMO1	C1136T	RS7501331	CC	- -	

Legend

- No effect
- Pay attention
- Pay close attention
- - - Wild type
- - + Heterozygous
- + + Homozygous

Gene description

Betacarotene monoxygenase 1 (BCMO1) codes for an enzyme that converts betacarotene into retinal, which is subsequently converted to vitamin A in the form of retinol or retinoic acid. Betacarotene is the most abundant provitamin A carotenoid in the diet and must be converted to retinol to support vital functions including vision, embryonic development, immunity, and cellular and skin health. Carotenoids are fat-soluble orange, yellow or red pigments commonly found in fruits and vegetables that can act as antioxidants or are converted to vitamin A. Humans are unable to synthesise vitamin A de novo, therefore they must consume foods with preformed vitamin A or provitamin A carotenoids. Genetic variations within BCMO1 that have been shown to reduce enzyme activity, referred to as poor converters, may increase an individual's dietary requirements for vitamin A. Studies indicate that BCMO1 is activated by iron and inhibited by copper. In addition, curcumin, rahmnetin (flavonol) and BHT (food additive) reduce BCMO1 activity.

Level of evidence star rating

★★★
Evidence relating the T alelle with reduced conversion of ÃŸ-carotene to retinol

★★★
Evidence relating the T allele and reduced vitamin A levels

What do your results mean?

The CC genotype is associated with normal enzyme activity and normal conversion of betacarotene to retinol. Research suggests the CC genotype may reduce risk of age-related macular degeneration.

Vitamin B12 Absorption And Transport > FUT2

Gene	Gene variation	rs number	Result	Effect
FUT2	G428A	rs601338	GA - +	

Legend

No effect

Pay attention

Pay close attention

- - Wild type

- + Heterozygous

+ + Homozygous

Gene description

Fucosyltransferase 2 (FUT2) codes for an enzyme involved in the synthesis of oligosaccharides and mediates the expression of gastrointestinal mucosal ABO (blood group) antigens. Oligosaccharides secreted in the intestinal mucosa feed intestinal flora, thereby directly influencing microbial concentrations and diversity. A genetic variation (rs601338) that changes G to A influences secretor status. Those with the GG or AG (wild-type heterozygous) are FUT2 secretors. FUT2 secretor status is associated with gastrointestinal (GIT) bacterial diversity and intestinal integrity, which can influence GIT function and nutrient absorption. FUT2 G allele is associated with lower vitamin B12 levels and may increase the risk of vitamin B12 deficiency.

Level of evidence star rating

★★
Evidence relating the rs601338 A allele with reduced diversity and abundance of beneficial bacteria

★★★★
Evidence relating the rs601338 A allele and increased vitamin B12 levels

What do your results mean?

The FUT2 rs601338 GG and AG genotypes (wild-type and heterozygous) secrete oligosaccharides/ABO (blood group) antigens on the gastrointestinal mucosa. Healthy individuals with the FUT2 G allele have been shown to have increased probiotic bacteria such as lactobacillus and bifidobacteria. However, secreted antigens also mediate the adhesion of various gastric pathogens, which may cause vitamin malabsorption. Lower B12 levels are associated with secretor status (AG and GG genotypes) compared to the AA genotype.

Vitamin B12 Absorption And Transport > FUT2

Gene	Gene variation	rs number	Result	Effect
FUT2	G772A	rs602662	GA - +	

Legend

- No effect
- Pay attention
- Pay close attention

- - Wild type
- - + Heterozygous
- + + Homozygous

Gene description

Fucosyltransferase 2 (FUT2) codes for an enzyme involved in the synthesis of oligosaccharides and mediates the expression of gastrointestinal mucosal ABO (blood group) antigens. Oligosaccharides secreted in the intestinal mucosa feed intestinal flora, thereby directly influencing microbial concentrations and diversity. A genetic variation (rs601338) that changes G to A influences secretor status. Those with the GG or AG (wild-type heterozygous) are FUT2 secretors. FUT2 secretor status is associated with gastrointestinal (GIT) bacterial diversity and intestinal integrity, which can influence GIT function and nutrient absorption. FUT2 G allele is associated with lower vitamin B12 levels and may increase the risk of vitamin B12 deficiency.

Level of evidence star rating

★★★★
Evidence relating the rs602662 A allele and increased vitamin B12 levels

What do your results mean?

The FUT2 G allele is associated with lower vitamin B12 levels and therefore carriers are likely to be at an increased risk of vitamin B12 deficiency as well as hyperhomocysteinemia. In particular, those who follow a vegetarian diet or have a low vitamin B12 intake are at increased risk for vitamin B12 deficiency and associated health disorders.

Vitamin B12 Absorption And Transport > TCN2

Gene	Gene variation	rs number	Result	Effect
TCN2	C776G	rs1801198	GG + +	

Legend

- No effect
- Pay attention
- Pay close attention
- - - Wild type
- - + Heterozygous
- + + Homozygous

Gene description

Transcobalamin 2 (TCN2) codes for a vitamin B12 (cobalamin) transport protein. TCN2 binds to vitamin B12 in the blood stream, transporting it to target cells and tissues. TCN2 also facilitates vitamin B12 transport into cells. Approximately 30% of plasma vitamin B12 is bound to TCN2 and it is responsible for the majority of B12 transport into tissues. TCN2 C776G has been shown to affect transcobalamin, vitamin B12 and homocysteine levels. Elevated homocysteine levels are associated with a number of health disorders and increased susceptibility to migraines. An interaction of this genetic variation with other variations in the folate, methionine-homocysteine, and vitamin B12 pathway (e.g. MTHFR, MTRR, MTR and FUT2) should be considered when interpreting the results. Please note that normal functioning of a protein or enzyme requires adequate nutrient levels and lifestyle modifications, irrespective of a variant being present.

Level of evidence star rating

★★
Evidence relating the G allele and lower cellular B12 levels

★★
Evidence relating the G allele and reduced vitamin B12 transport

What do your results mean?

The TCN2 G allele is associated with reduced vitamin B12 transport into cells, which may result in higher B12 blood levels and lower cellular levels compared to the CC genotype (wild-type). The GG genotype is more susceptible to increased homocysteine levels compared to the wild-type genotype when serum vitamin B12 and holo-transcobalamin (trancobalamin-vitamin B12 complex) levels are low. The TCN2 G allele may increase the risk for vitamin B12 associated health disorders.

Vitamin C Transport > SLC23A1

Gene	Gene variation	rs number	Result	Effect
SLC23A1	G790A	rs33972313	GG - -	

Legend

- No effect
- Pay attention
- Pay close attention
- - - Wild type
- - + Heterozygous
- + + Homozygous

Gene description

The solute carrier family 23 member 1 (SLC23A1) gene codes for a sodium-dependent vitamin C transport protein. This transport protein plays an essential role in hepatic portal absorption and renal reabsorption of vitamin C, therefore helping to regulate vitamin C levels. SLC23A1 facilitates the transport and absorption of vitamin C across the cell membrane into cells and target tissues. SLC23A1 is predominantly expressed in the liver, small intestine, colon, kidneys and ovaries. Vitamin C, also known as ascorbate or L-ascorbic acid, is an essential part of the human diet and low levels have been associated with a wide range of complex chronic health disorders. Vitamin C is a potent antioxidant and is required for the synthesis of various compounds such as collagen, carnitine, catecholamines and bile acid. In addition, vitamin C enhances the absorption of vitamins and minerals such as iron and folate. Individuals who inherit the genetic variation rs33972313 associated with lower vitamin C levels, and who have a poor diet and lifestyle factors such as smoking and alcohol intake that reduce vitamin C levels, may be at increased risk for vitamin C deficiency.

Level of evidence star rating

★★★★
Evidence relating the A allele and reduced vitamin C levels

What do your results mean?

The GG genotype is associated with normal vitamin C transport and reduced risk of low vitamin C levels compared to the GA and AA genotypes.

Vitamin D > DHCR7

Gene	Gene variation	rs number	Result	Effect
DHCR7	G>T	rs12785878	TT + +	

Legend

- No effect
- Pay attention
- Pay close attention

- - Wild type
- - + Heterozygous
- + + Homozygous

Gene description

The 7-dehydrocholesterol reductase (DHCR7) gene codes for an enzyme that converts 7-dehydrocholesterol (7-DHC) into cholesterol; this is the final step required for cholesterol production. 7-DHC is also a precursor of vitamin D and can be found in abundance in the skin. When sunlight penetrates the skin, 7-DHC is converted to pre-vitamin D, which in-turn can be converted to active vitamin D. DHCR7 plays an important role in regulating the production of cholesterol and vitamin D, with increased enzyme activity pushing the precursor away from vitamin D synthesis. A genetic variation within DHCR7 (rs12785878) has been associated with vitamin D deficiency. Research indicates that a combination of genetic variations in CYP2R, GC and DHCR7 may increase the risk and severity of vitamin D deficiency. Therefore, individuals who inherit the DHCR7 G allele should review the other vitamin D related genes and discuss further investigations to determine individual susceptibility to vitamin D deficiency. Research demonstrates a common disinfectant, benzalkonium chloride (BAC), found in eye, nose and ear drops and sprays, shampoo, hand sanitisers, wet wipes, deodorants, throat lozenges, mouthwash, cold sore creams and surface disinfectants, can inhibit DHCR7 activity at non-cytotoxic concentrations.

Level of evidence star rating

★★★
Evidence relating to BAC enzyme inhibition

★★★★
Evidence relating the G allele with increased risk for vitamin D deficiency

What do your results mean?

The TT genotype is associated with increased levels of vitamin D compared to the GT and GG genotypes.

Vitamin D > CYP2R1

Gene	Gene variation	rs number	Result	Effect
CYP2R1	G>A	rs10741657	GG + +	

Legend

- No effect
- Pay attention
- Pay close attention

- - Wild type
- - + Heterozygous
- + + Homozygous

Gene description

The cytochrome P450 2R1 (CYP2R1) gene codes for an enzyme that converts vitamin D obtained from sunlight, the diet and supplements into 25-hydroxy vitamin D (25-OH D). 25-OH D is the major circulating form of vitamin D and acts as a precursor for the active form of vitamin D. The synthesis of active vitamin D involves multiple enzyme reactions that occur in different tissues. CYP2R1, also known as vitamin D 25-hydroxylase, regulates the conversion of the inactive form of vitamin D in the liver. Genetic variations within CYP2R1 have been associated with reduced levels of serum 25-OH D. Research suggests that a combination of genetic variations in CYP2R1 (GC and DHCR7) may increase the risk of vitamin D deficiency. In addition, G allele carriers may be more susceptible to autoimmune conditions and exhibit reduced efficacy towards vitamin D supplementation. Individuals who inherit the genetic variation within CYP2R1 should review the other vitamin D related genes and discuss further investigations to determine individual susceptibility to vitamin D deficiency.

Level of evidence star rating

★★★
Evidence relating the GG genotype with reduced response to vitamin D supplementation

★★★★
Evidence relating the G allele with increased risk for vitamin D deficiency

What do your results mean?

The G allele is associated with increased risk for vitamin D deficiency. Individuals with one or more G alleles are shown to be approximately 3.7 times more likely to be vitamin D deficient compared to the AA genotype. Individuals carrying the GG genotype may have a reduced response to vitamin D supplementation. Therefore those who are low in vitamin D may require higher doses of vitamin D supplementation.

Vitamin D > CYP27B1

Gene	Gene variation	rs number	Result	Effect
CYP27B1		rs4646536	TT + +	

Legend

- No effect
- Pay attention
- Pay close attention

- - Wild type
- - + Heterozygous
- + + Homozygous

Gene description

The cytochrome P450 27B1 (CYP27B1) gene codes for an enzyme that converts the major circulating form of vitamin D, referred to as 25-hydroxy vitamin D (25-OH D), into the active form of vitamin D 1,25-hydroxy vitamin D (1,25-OH D). Active vitamin D is involved in calcium homeostasis, cell proliferation and regulation of the immune system. Although CYP27B1 is primarily expressed in the kidney, extra-renal production of active vitamin D has been demonstrated in tissues such as the lymph and skin. Renal CYP27B1 is upregulated by parathyroid hormone (PTH) when serum calcium is low. The boost in active vitamin D production increases calcium bone resorption and, as a feedback effect, active vitamin D in-turn inhibits PTH. In addition, calcitonin and insulin-like growth factor 1 (IGF-1) can also stimulate renal CYP27B1 enzyme activity. In contrast, CYP27B1 produced by macrophages is not suppressed by elevated active vitamin D levels, but instead is upregulated by immune stimuli. Genetic variations that reduce CYP27B1 enzyme activity and low levels of vitamin D have been associated with increased risk for autoimmune disorders. Reduced CYP27B1 enzyme activity would ultimately result in lower active vitamin D (1,25-OH D). However this gene is tightly regulated by various mechanisms and 1,25-OH D is difficult to measure, therefore current research does not show a direct link with active vitamin D levels. Individuals who inherit the genetic variation within CYP27B1 should review the other vitamin D related genes and discuss further investigations to determine vitamin D levels.

Level of evidence star rating

★★
Evidence relating the T allele with increased susceptibility to Hashimotoâ€™s

★★
Evidence relating the T allele with increased susceptibility to Type 1 Diabetes

What do your results mean?

The T allele is associated with increased susceptibility to autoimmune disorders, which may be due to reduced CYP27B1 enzyme activity.

Vitamin D > GC

Gene	Gene variation	rs number	Result	Effect
GC	A>C	rs2282679	CA - +	

Legend

 **No effect**

 **Pay attention**

 **Pay close attention**

- - **Wild type**

- + **Heterozygous**

+ + **Homozygous**

Gene description

The GC-globulin (GC) gene codes for the vitamin D binding protein (DBP). DBP binds to vitamin D, in particular 25-OH vitamin D, in order to transport vitamin D and its metabolites to target tissues such as the skin, liver and kidneys. DBP is the primary vitamin D transporter and plays a role in maintaining the total levels of vitamin D and regulating the amounts of free (unbound) vitamin D available for specific cells and tissues. The major proportion of vitamin D in the blood is bound to this transport protein. DBP may have immune functions independent of its role as a transporter of vitamin D. A genetic variation within GC (rs2282679) has been suggested to affect the ability of DBP to bind to vitamin D. Carriers of genetic variations within GC have been shown to have lower levels of vitamin D and are therefore at an increased risk of vitamin D insufficiency. Research indicates a lower frequency of the C allele carriers in Africans and American Africans. Individuals who inherit the genetic variation within GC should review the other vitamin D related genes and discuss further investigations to determine susceptibility to vitamin D insufficiency.

What do your results mean?

The C allele is associated with reduced vitamin D binding affinity to DBP, which may impact on vitamin D transport to target tissues. Individuals who inherit the CA genotype have a modest risk of vitamin D insufficiency compared to the AA genotype.

Vitamin D > VDR

Gene	Gene variation	rs number	Result	Effect
VDR	FOK	rs2228570	TC - +	

Gene description

The vitamin D receptor (VDR) gene codes for a transcription factor that binds to the active form of vitamin D, 1-25-(OH)D and mediates its biological functions. VDR and vitamin D form a complex with the retinoid-X receptor, which binds to vitamin D response elements on DNA, modulating gene expression and transcription. Research indicates the VDR and vitamin D complex regulates the expression of more than 900 genes involved in a wide range of physiological functions. VDR contains a zinc finger-binding domain and is closely related to the thyroid hormone receptors. It is expressed in most tissues including the intestines and the brain. Glucocorticoids have been shown to decrease VDR expression. The FOK1 genetic variation within VDR affects the length and functional activity of the VDR protein. FOK1 has been associated with bone mineralisation, fracture risk and 25-(OH)D levels. Research has shown that C allele carriers have reduced vitamin D levels and therefore may be at risk of vitamin D insufficiency. Individuals who inherit the FOK1 variant should review the other vitamin D related genes and discuss further investigations to determine individual susceptibility to vitamin D insufficiency.

Level of evidence star rating

★★
Evidence relating the C allele and reduced vitamin D levels

What do your results mean?

The C allele is associated with reduced levels of vitamin D (25-(OH) D) compared to TT genotype carriers and may therefore increase the risk of vitamin D insufficiency.

Legend

- No effect
- Pay attention
- Pay close attention

- - Wild type
- - + Heterozygous
- + + Homozygous

Vitamin D > CYP24A1

Gene	Gene variation	rs number	Result	Effect
CYP24A1	T>A	rs6013897	AA + +	

Legend

- No effect
- Pay attention
- Pay close attention
- - - Wild type
- - + Heterozygous
- + + Homozygous

Gene description

The cytochrome P450 24A1 (CYP24A1) gene codes for an enzyme that degrades (inactivates) the active form of vitamin D, 1,25-OH vitamin D, helping to regulate the levels of active vitamin D. The degraded vitamin D is then excreted through the bile. In addition, CYP24A1 degrades and inactivates the precursor of active vitamin D, 25-OH vitamin D, when there is sufficient production of the active form. In regulating the levels of vitamin D, this enzyme plays a role in calcium homeostasis, immune support and the vitamin D endocrine system. CYP24A1 is expressed in the kidney and all vitamin D target tissues, except for the the liver and osteoclasts. A genetic variation in CYP24A1 (rs6013897) results in a marginal reduction in circulating vitamin D levels. However, on its own, this genetic variation is not a causal factor for vitamin D deficiency. Individuals who inherit the genetic variation within CYP24A1 that is associated with lower vitamin D levels should review the other vitamin D related genes and discuss further investigations to determine vitamin D levels.

Level of evidence star rating

★★★★
Evidence relating the A allele with marginally reduced vitamin D levels

★★★★
Evidence relating the A allele with reduced response to vitamin D supplementation

What do your results mean?

The A allele is associated with marginally reduced vitamin D levels compared to those with the TT genotype. Furthermore, A allele carriers exhibit a reduced response to vitamin D supplementation, with homozygotes (AA) being less responsive than heterozygotes (AT).

Folate Pathway > MTHFD1

Gene	Gene variation	rs number	Result	Effect
MTHFD1	G1958A	rs2236225	AA + +	

Legend

- No effect
- Pay attention
- Pay close attention

- - Wild type
- - + Heterozygous
- + + Homozygous

Gene description

Methylene tetrahydrofolate dehydrogenase 1 (MTHFD1) codes for an enzyme that catalyses three sequential reactions resulting in various forms of folate that support DNA synthesis and repair, homocysteine metabolism and methylation. Reduced MTHFD1 activity, in association with low folate and/or low choline, may increase the risk for genome damage and folate associated health disorders. Please note that normal functioning of a protein or enzyme requires adequate nutrient levels and lifestyle modifications, irrespective of a variant being present.

Level of evidence star rating

★★★
The A allele is associated with a reduced MTHFD1 enzyme activity

What do your results mean?

The MTHFD1 A allele is associated with reduced enzyme activity and may increase the risk for choline deficiency compared to the GG genotype. The AA genotype is associated with approximately 40% reduction in enzyme activity, while the GA genotype has a minor effect. Reduced MTHFD1 enzyme activity may impact on DNA synthesis and homocysteine metabolism, depending on nutrient intake. Studies suggest the A allele may be associated with increased risk for pregnancy complications in the presence of low folate, choline and B vitamins.

Folate Pathway > MTHFD1

Gene	Gene variation	rs number	Result	Effect
MTHFD1	C105T	rs1076991	TT + +	

Legend

- No effect
- Pay attention
- Pay close attention

- - Wild type
- - + Heterozygous
- + + Homozygous

Gene description

Methylene tetrahydrofolate dehydrogenase 1 (MTHFD1) codes for an enzyme that catalyses three sequential reactions resulting in various forms of folate that support DNA synthesis and repair, homocysteine metabolism and methylation. Reduced MTHFD1 activity, in association with low folate and/or low choline, may increase the risk for genome damage and folate associated health disorders. Please note that normal functioning of a protein or enzyme requires adequate nutrient levels and lifestyle modifications, irrespective of a variant being present.

Level of evidence star rating

★★
The T allele is associated with reduced MTHFD1 enzyme activity

What do your results mean?

Currently there is limited evidence for this MTHFD1 SNP. One in vitro study has shown the T allele is linked with reduced enzyme activity and the TT genotype, when inherited with the MTHFD1 1958 AA genotype, may increase the risk for neural tube defects, suggesting folate metabolism may be disrupted.

Folate Pathway > SHMT1

Gene	Gene variation	rs number	Result	Effect
SHMT1	C1420T	rs1979277	CT - +	

Legend

- No effect
- Pay attention
- Pay close attention

- - Wild type
- - + Heterozygous
- + + Homozygous

Gene description

Serine hydroxymethyltransferase 1 (SHMT1) codes for a pyridoxal phosphate (vitamin B6)-containing enzyme that catalyses the reversible conversion of serine and tetrahydrofolate (THF) to glycine and 5,10-methylenetetrahydrofolate (5,10-MTHF). SHMT1 supports DNA synthesis and repair, and homocysteine metabolism. Reduced vitamin B6 may decreases SHMT1 activity and studies suggest iron may increase SHMT1 activity. Please note that normal functioning of a protein or enzyme requires adequate nutrient levels and lifestyle modifications, irrespective of a variant being present.

Level of evidence star rating

★★
Evidence relating the T allele and increased Homocysteine levels

What do your results mean?

The SHMT T allele may reduce enzyme activity. One study suggests the T allele is associated with impaired remethylation of homocysteine to methionine. In addition, SHMT 1420 T and MTHFR 677 T may have a combined effects, resulting in increased homocysteine. Currently there is limited evidence relating genetic variations within SHMT and health outcomes.

Folate Pathway > MTHFR

Gene	Gene variation	rs number	Result	Effect
MTHFR	C677T	rs1801133	CT - +	

Legend

- No effect
- Pay attention
- Pay close attention
- - - Wild type
- - + Heterozygous
- + + Homozygous

Gene description

Methylenetetrahydrofolate reductase (MTHFR) codes for the enzyme that converts one form of folate 5,10-methylenetetrahydrofolate (5,10-MTHF) to 5-methyltetrahydrofolate (5-MTHF). MTHFR directs folate away from DNA synthesis towards homocysteine metabolism supporting methylation. 5-MTHF provides the methyl group required to convert homocysteine to methionine. Methionine is an essential amino acid necessary for protein synthesis and the production of S-adenosylmethionine (SAMe). SAMe provides the methyl groups for methylation reactions throughout the body. Low folate and low riboflavin (vitamin B2) are associated with reduced MTHFR activity and may result in increased homocysteine levels, i.e. hyperhomocysteinemia. Endothelial injury, as a result of hyperhomocysteinemia, can lead to inflammation, oxidative stress and reduced bioavailability of nitric oxide (NO) thereby affecting vascular function and blood clotting. These changes have been associated with various health outcomes such as CVD, neurological disorders, pregnancy complications and in the initiation and maintenance of migraine episodes as well as the characteristic symptoms in patients experiencing migraine with aura. Please note that normal functioning of a protein or enzyme requires adequate nutrient levels and lifestyle modificiations, irrespective of a variant being present.

Level of evidence star rating

★★★
The T allele is associated wth reduced MTHFR enzyme activity

★★★★★
The T allele is associated with reduced folate levels and increased Homocysteine

What do your results mean?

The MTHFR 677 CT genotype is associated with approximately 30% reduced enzyme activity compared to the CC genotype. Reduced MTHFR enzyme activity indicates increased homocysteine, altered methylation and possible increased risk for various health conditions, particularly in the presence of low folate and other B vitamins.

Folate Pathway > MTHFR

Gene	Gene variation	rs number	Result		Effect
MTHFR	A1298C	rs1801131	AA	- -	

Legend

- No effect
- Pay attention
- Pay close attention
- - - Wild type
- - + Heterozygous
- + + Homozygous

Gene description

Methylenetetrahydrofolate reductase (MTHFR) codes for the enzyme that converts one form of folate 5,10-methylenetetrahydrofolate (5,10-MTHF) to 5-methyltetrahydrofolate (5-MTHF). MTHFR directs folate away from DNA synthesis towards homocysteine metabolism supporting methylation. 5-MTHF provides the methyl group required to convert homocysteine to methionine. Methionine is an essential amino acid necessary for protein synthesis and the production of S-adenosylmethionine (SAMe). SAMe provides the methyl groups for methylation reactions throughout the body. Low folate and low riboflavin (vitamin B2) are associated with reduced MTHFR activity and may result in increased homocysteine levels, i.e. hyperhomocysteinemia. Endothelial injury, as a result of hyperhomocysteinemia, can lead to inflammation, oxidative stress and reduced bioavailability of nitric oxide (NO) thereby affecting vascular function and blood clotting. These changes have been associated with various health outcomes such as CVD, neurological disorders, pregnancy complications and in the initiation and maintenance of migraine episodes as well as the characteristic symptoms in patients experiencing migraine with aura. Please note that normal functioning of a protein or enzyme requires adequate nutrient levels and lifestyle modificiations, irrespective of a variant being present.

Level of evidence star rating

★★
The C allele is associated with MTHFR enzyme activity

★★★
The C allele is associated with reduced folate levels ad increased homocysteine

What do your results mean?

The MTHFR 1298 AA genotype is associated with normal enzyme activity.

Homocysteine-Methionine Pathway > MTR

Gene	Gene variation	rs number	Result	Effect
MTR	A2756G	rs1805087	AA - -	

Gene description

Methionine synthase (MTR) codes for the enzyme that converts homocysteine into methionine. Methionine is an essential amino acid necessary for protein synthesis and the production of S-adenosylmethionine (SAMe). SAMe provides the methyl groups for methylation reactions throughout the body. Vitamin B12, specifically methyl-B12, and zinc are required for optimal MTR activity and methionine production. Low vitamin B12 levels are associated with reduced MTR activity. MTR is expressed in the brain, heart, pancreas, skeletal muscle and placenta and at lower levels in the lungs, liver and kidneys. Studies suggest that alcohol, mercury and nitrous oxide may reduce or inhibit methionine synthase, consequently impacting on methylation reactions. Suboptimal MTR activity may affect homocysteine levels. Hyperhomocysteinemia can result in endothelial damage leading to inflammation and oxidative stress, which may effect vascular function. Please note that normal functioning of a protein or enzyme requires adequate nutrient levels and lifestyle modifications, irrespective of a variant being present.

Level of evidence star rating

★★
The G allele is associated with a slight decrease in homocysteine and altered methylation

What do your results mean?

The MTR 2756 AA genotype is associated with a slight increase in homocysteine levels compared to the GG genotype, suggesting slower enzyme activity.

Legend

- No effect
- Pay attention
- Pay close attention
- - Wild type
- - + Heterozygous
- + + Homozygous

Homocysteine-Methionine Pathway > MTRR

Gene	Gene variation	rs number	Result	Effect
MTRR	A66G	rs1801394	AA - -	

Legend

- No effect
- Pay attention
- Pay close attention
- - - Wild type
- - + Heterozygous
- + + Homozygous

Gene description

Methionine synthase reductase (MTRR) codes for the enzyme that regenerates vitamin B12 into the methylated form methyl-B12 (methylcobalmin), which acts as a cofactor for methionine synthase (MTR). Therefore, MTR and MTRR work together to convert homocysteine into methionine, which is dependent on vitamin B12 levels. MTRR also requires riboflavin (vitamin B2) for optimal enzyme activity. Suboptimal MTRR activity may increase homocysteine levels, i.e. hyperhomocysteinemia. Endothelial injury, as a result of hyperhomocysteinemia, can lead to inflammation, oxidative stress and reduced bioavailability of nitric oxide (NO), thereby affecting vascular function and blood clotting. An interaction between MTRR A66G with other genetic variations in the folate, methionine-homocysteine and vitamin B12 pathway (e.g. MTHFR C677T and MTR A2756G) is likely. Current research indicates no direct association of this genetic variant with migraine susceptibility. However, this genetic variation may alter the response to the use of folate, vitamin B6 and vitamin B12 supplementation as migraine treatment. Please note that normal functioning of a protein or enzyme requires adequate nutrient levels and lifestyle modifications, irrespective of a variant being present.

Level of evidence star rating

★
The G allele is associated with reduced MTRR enzyme activity

★★
The G allele is associated increasing the risk of higher homocysteine levels and altered methylation

What do your results mean?

The AA genotype is associated with normal enzyme activity.

Homocysteine-Methionine Pathway > BHMT

Gene	Gene variation	rs number	Result	Effect
BHMT	G742A	rs3733890	GG - -	

Legend

- No effect
- Pay attention
- Pay close attention
- - - Wild type
- - + Heterozygous
- + + Homozygous

Gene description

Betaine homocysteine methyltransferase (BHMT) codes for a zinc-dependent enzyme that converts betaine and homocysteine to dimethylglycine and methionine. Choline acts as a methyl donor, via oxidation to betaine. BHMT activity is found at high levels in the liver and kidney, with low levels in the brain and other tissues. Transsulfuration and methionine pathways do not have the capacity to remove excess homocysteine when BHMT is not present, indicating the enzyme plays an important role in the homoeostasis of homocysteine. BHMT is upregulated when the methylenetetrahydrofolate reductase (MTHFR) pathway is restricted and folate levels are low. Please note that normal functioning of a protein or enzyme requires adequate nutrient levels and lifestyle modifications, irrespective of a variant being present.

Level of evidence star rating

★★★
Evidence relating the A allele and reduced levels of dimethylglycine (DMG)

What do your results mean?

The BHMT GG genotype is associated with normal enzyme function.

Transsulfuration Pathway > CBS

Gene	Gene variation	rs number	Result	Effect
CBS	C699T	rs234706	CC - -	

Legend

- No effect
- Pay attention
- Pay close attention

- - Wild type
- - + Heterozygous
- + + Homozygous

Gene description

Cystathionine beta synthase (CBS) codes for a haem-containing enzyme that requires serine and vitamin B6 to convert homocysteine into cystathionine, the precursor for cysteine and glutathione. CBS is the first enzyme in the transsulfuration pathway and directs homocysteine away from methionine synthesis. Low methionine can down-regulate CBS activity, which may impact on glutathione production. CBS activity produces hydrogen sulfide, which can protect the brain from hypoxia. Research suggests that CBS regulation in the kidneys may be testosterone-dependent and contributes to sex-dependent differences in homocysteine levels. CBS is expressed in the liver, brain, heart, lungs, kidneys and pancreas in adults. In the foetus it is expressed in the brain, liver and kidneys. Please note that normal functioning of a protein or enzyme requires adequate nutrient levels and lifestyle modifications, irrespective of a variant being present.

Level of evidence star rating

★★★
Evidence relating the T allele and folate supplementation with increased rate of lowering of Homocysteine

★★★
Evidence relating the T allele and lower Homocysteine levels

What do your results mean?

CBS CC genotype is associated with increased homocysteine levels, reduced cystathionine and reduced betaine levels, suggesting lower enzyme activity compared to the TT genotype. Cystathionine is a precursor for glutathione, therefore CBS activity may impact on glutathione production and detoxification processes.

Fatty Acid Related Genes > PEMT

Gene	Gene variation	rs number	Result	Effect
PEMT	G>A	rs7946	GA - +	

Legend

No effect

Pay attention

Pay close attention

- - Wild type

- + Heterozygous

+ + Homozygous

Gene description

Phosphatidylethanolamine N-methyltransferase (PEMT) codes for an enzyme that catalyses the de novo synthesis of choline, via methylation of phosphatidylethanolamine, to form phosphatidylcholine. Choline is an essential nutrient needed for cell membranes, cell signalling and lipid transport. Choline is also a precursor to the neurotransmitter acetylcholine and the methyl donor betaine. Folate and choline are tightly linked through the methylation pathway and processes within the body. PEMT is regulated by oestrogen and studies show that premenopausal women with higher oestrogen levels are at reduced risk for choline deficiency. Choline, via dimethylglycine (DMG) production, contributes to glycine for glutathione production during foetal development. Individuals who inherit genetic variations within PEMT, that are associated with lower choline, should review the other choline-related genes BHMT and MTHFD1.

Level of evidence star rating

★★
Evidence relating the A allele and increased risk for low choline levels

★★★
The A allele is associated with reduced MTHFD1 enzyme activity

What do your results mean?

The A allele is associated with reduced enzyme activity. The AA genotype reduces activity by approximately 30-40% and GA to a lesser extent. The A allele may decrease the ability to generate choline de novo, thus increasing dependency on dietary choline. The A allele in individuals with adequate choline is thought to spare methyl groups and protect against some disease, such as malaria, that require choline for parasite replication. Studies suggest that individuals who are low in the nutrients choline, betaine and folate and have inherited the PEMT GA or AA genotype are at increased risk for choline deficiency and associated health disorders. Choline deficiency has been associated with non-alcoholic fatty liver disease, impaired foetal development and neurological conditions. Ensure adequate choline intake, particularly during times of higher need such as pregnancy, breastfeeding and after menopause.

Fatty Acid Related Genes > FADS1

Gene	Gene variation	rs number	Result	Effect
FADS1	C53T	rs174546	CT - +	

Legend

- No effect
- Pay attention
- Pay close attention

- - Wild type
- - + Heterozygous
- + + Homozygous

Gene description

Fatty acid desaturase 1 (FADS1) codes for an enzyme involved in omega-6 and omega-3 fatty acid metabolism. Specifically, FADS1 converts omega-6 into arachidonic acid (AA) and omega-3 into eicosapentaenoic acid (EPA). AA and EPA are precursors for eicosanoids that are involved in regulating cell growth, muscle repair and activity, blood clotting, neurological development and neurological health, as well as secretion of hormones. AA is metabolised to both pro-inflammatory and anti-inflammatory eicosanoids during and after an inflammatory response. While EPA, the precursor to docosahexaenoic acid (DHA), is metabolised into anti-inflammatory compounds. The levels of these fatty acids are dependent on dietary intake and genetic variations within FADS1 that alter enzyme activity and influence the production of AA and EPA. The western diet is high in omega-6 and low in omega-3 resulting in increased risk for chronic inflammation. Increasing dietary intake of omega-3 results in a replacement of omega-6 decreasing the production of AA-derived pro-inflammatory mediators that are involved in the pathogenesis of various health disorders, including migraines. To date, no studies have investigated the link between the FADS1 genetic variation and migraine susceptibility, however increased dietary intake of omega-3, particularly DHA and EPA, has shown to reduce migraine duration and possibly frequency and severity in migraine sufferers. Furthermore, omega-3 has been shown to suppress nitric oxide production, which is also believed to play an important role in the development of migraine symptoms.

Level of evidence star rating

★★★
Evidence relating the T allele and increased triglycerides and LDL cholesterol

★★★
Evidence relating the T allele with reduced enzyme activity and lower levels of the omega 6 fatty acid AA and the omega 3 fatty acid EPA

★★★★
Evidence relating the T allele with higher waist circumference and Body Mass Index

What do your results mean?

The CT genotype is associated with intermediate enzyme activity and lower levels of the omega-6, AA and omega-3 EPA compared to the wildtype genotype (CC). The CT genotype is also associated with increased triglycerides and LDL cholesterol.

Phase 1 Detox-related Genes > CYP17A1

Gene	Gene variation	rs number	Result		Effect
CYP17A1	T-34C	rs743572	AG	- +	

Legend

- No effect
- Pay attention
- Pay close attention
- - - Wild type
- - + Heterozygous
- + + Homozygous

Gene description

Cytochrome P450 17A1 (CYP17A1) is a key enzyme for the production of androgens. CYP17A1 converts pregnenolone and progesterone into DHEA and androstenedione, the precursors to testosterone and oestrogen. CYP17A1 codes for a hydroxylase enzyme that produces 17-OH pregnenolone and 17-OH progesterone, as well as a lyase enzyme that goes on to produce DHEA and androstenedione. Altered CYP17A1 activity has been associated with changes in androgen and oestrogen levels, as well as hormone-related disorders. Individuals who inherit genetic variations within CYP17A1, that increase enzyme activity, should review other hormone related genes such as CYP19A1, CYP1B1 and COMT.

Level of evidence star rating

★★
Evidence relating the G allele and polycystic ovarian syndrome (PCOS)

★★★
Evidence relating the G alelle and uterine fibroids

★★★
Evidence relating the G allele and increased oestrogen levels

What do your results mean?

The G allele has been associated with increased enzyme activity and increased oestrogen levels. Increased enzyme activity and exposure to sex hormones may increase risk for hormone-sensitive disorders such as polycystic ovarian syndrome (PCOS).

Phase 1 Detox-related Genes > CYP19A1

Gene	Gene variation	rs number	Result	Effect
CYP19A1	C19T	rs10046	CC - -	

Gene description

Cytochrome P450 19A1 (CYP19A1) codes for the aromatase enzyme that converts androstenedione to oestrone (E1) and testosterone to oestradiol (E2). Aromatase activity has been shown to be increased by a number of factors including alcohol and obesity. In addition, reduced activity has been linked to glyphosate. Altered aromatisation may lead to changes in oestrogen levels and the risk for hormone-sensitive disorders. Individuals who inherit genetic variations within CYP19A1, that increase enzyme activity, should review other hormone related genes such as CYP17A1, CYP1B1 and COMT.

What do your results mean?

The CC genotype is associated with normal enzyme activity.

Legend

- No effect
- Pay attention
- Pay close attention

- - Wild type
- \+ Heterozygous
- \+ \+ Homozygous

Phase 1 Detox-related Genes > CYP1A1

Gene	Gene variation	rs number	Result	Effect
CYP1A1	A2455G	rs1048943	AA - -	

Legend

- No effect
- Pay attention
- Pay close attention
- - - Wild type
- - + Heterozygous
- + + Homozygous

Gene description

CYP1A1 metabolises oestrone (E1) and oestradiol (E2) into the 2-hydroxy metabolites, 2OH-E1 and 2OH-E2. CYP1A1 also metabolises environmental pollutants, including polycyclic aromatic hydrocarbons (PAHs), which are released from substances such as cigarette smoke, car exhaust fumes and chargrilled meats. Genetic variations that increase enzyme activity may increase the amount of 2OH oestrogen metabolites as well as potentially toxic and reactive metabolites from environmental pollutants. The 2OH oestrogen metabolites are considered less harmful than the 4OH and 16OH metabolites. Individuals who inherit genetic variations within CYP1A1, which increase enzyme activity, should review the other hormone-related genes such as CYP17A1, CYP19A1, MTHFR and COMT and/or CYP1B1 that also metabolise PAHs.

Level of evidence star rating

★★
Evidence relating the G allele and risk for uterine fibroids

★★
Evidence relating the G allele with increased risk for reduced sperm motility

★★★
Evidence relating the G allele with increased enzyme activity and conversion of oestrogen to catechol oesotrogensÂ

★★★
Evidence relating the T allele with increased conversion of androgens to oestrogen

What do your results mean?

The AA genotype is associated with normal enzyme activity, and possibly lower levels of reactive metabolites, compared to those with the G allele.

Phase 1 Detox-related Genes > CYP1A1/1A2

Gene	Gene variation	rs number	Result	Effect
CYP1A1/1A2		rs2472297	CT - +	

Legend

- No effect
- Pay attention
- Pay close attention

- - Wild type
- - + Heterozygous
- + + Homozygous

Gene description

The cytochrome P450 1A2 (CYP1A2) gene codes for a phase 1 detoxification enzyme involved in the metabolism of endogenous substances and xenobiotics as well as the NADPH-dependent electron transport pathway. CYP1A2 catalyses many reactions involved in drug metabolism and the synthesis of cholesterol, steroid hormones and other lipids. In particular, CYP1A2 metabolises caffeine, oestrogen, melatonin and carcinogens such as quinoline and 2-aminofluorine. Vegetables such as cabbage, broccoli and cauliflower are known to increase CYP1A2 activity, whereas the spices cumin and turmeric inhibit enzyme activity. Other inducers include polycyclic hydrocarbons (PAHs), which are also present in coffee as a result of the roasting process, cigarette smoke, burnt (barbequed) meat and other foods, polychlorinated biphenyls (PCBs) and dioxin (TCDD). The majority of caffeine is metabolised to paraxanthine (or 17X) primarily by CYP1A2 in the liver. A genetic variation in CYP1A2 (rs2472297) has been identified in Europeans and individuals with European heritage, but not in Asians or Africans. The rs2472297 genetic variation in CYP1A2 is in linkage with another variation rs2470893, indicating the two variations are likely to be inherited together. Evidence for both variations suggests that they are associated with habitual coffee consumption. To date, no effect of rs2472297 on CYP1A2 enzyme activity has been established. However, research suggests that caffeine intake increases CYP1A2 activity, which makes a higher enzyme activity in T allele carriers plausible.

Level of evidence star rating

★★
Evidence relating the T allele with fast caffeine metabolism

★★★★
Evidence relating the T allele and increased coffee consumption

What do your results mean?

The CT and TT genotypes are consistently associated with higher coffee consumption compared to those with the CC genotype. The CT genotype is associated with a moderate increase in coffee consumption and the TT genotype is associated with the highest habitual coffee intake. The T allele is likely to be associated with the fast caffeine metaboliser phenotype.

Phase 1 Detox-related Genes > CYP2A6

Gene	Gene variation	rs number	Result	Effect
CYP2A6	A>T	rs1801272	AA - -	

Legend

- No effect
- Pay attention
- Pay close attention

- - Wild type
- - + Heterozygous
- + + Homozygous

Gene description

The cytochrome P450 2A6 (CYP2A6) gene codes for a phase 1 detoxification enzyme involved in the oxidation of tobacco, herbicides, pollutants and xenobiotics. CYP2A6 is the primary enzyme responsible for 80% of the inactivation of nicotine to cotinine. In addition, CYP2A6 is the only enzyme that is able to metabolise coumarin. Coumarin is found naturally in many plants, but high levels have been detected in tonka beans, cassia cinnamon (but not Ceylon cinnamon) and potentially some plants used for herbal medicine. A genetic variation in CYP2A6 (rs1801272) renders the enzyme unable to metabolise coumarin and has been associated with a reduced capacity to metabolise nicotine, but also affects smoking habits, nicotine dependence and strategies to quit smoking. Genetic variations within COMT have also been associated with smoking behaviour. Nicotine is known to stimulate the release of dopamine, which is involved in reward effects of smoking, and COMT is a key enzyme involved in the degradation of dopamine. Research suggests that individuals with reduced COMT activity (rs4680 Met/Met) and reduced CYP2A6 activity have lower risk for nicotine dependence and a better response to nicotine replacement therapy and smoking cessation.

Level of evidence star rating

★★★
Evidence relating the T allele and coumarin metabolismÂ

★★★
Evidence relating the T allele with increased likelihood to quit smoking successfully

★★★
Evidence relating the T allele with poor nicotine metabolism

★★★★
Evidence relating the T allele and reduced enzyme activity

What do your results mean?

The AA genotype is associated with normal enzyme activity. Those who inherit the AA genotype are fast metabolisers of nicotine compared to the AT and TT genotypes. Research suggests that smokers who inherit the AA genotype are likely to smoke more cigarettes a day, have more severe withdrawal symptoms and are less likely to quit when treated with nicotine replacement therapy compared to those with the T allele.

Phase 1 Detox-related Genes > CYP1B1

Gene	Gene variation	rs number	Result		Effect
CYP1B1	A10106G	rs1800440	AA	- -	

Legend

- No effect
- Pay attention
- Pay close attention
- - - Wild type
- - + Heterozygous
- + + Homozygous

Gene description

Cytochrome P450 enzyme 1B1 (CYP1B1) metabolises oestrone (E1) and oestradiol (E2) into the reactive 4-hydroxy metabolites, 4OH-E1 and 4OH-E2. CYP1B1 also metabolises environmental pollutants including polycyclic aromatic hydrocarbons (PAHs), which are released from burnt substances such as cigarette smoke, petroleum-related compounds and chargrilled meats. Genetic variations that increase enzyme activity may increase the amount of toxic and reactive metabolites that can impact both men and women's health. Individuals who inherit genetic variations within CYP1B1, that increase enzyme activity, should review the other hormone-related genes such as CYP17A1, CYP19A1, MTHFR and COMT, and/or CYP1A1 which also metabolises PAHs.

Level of evidence star rating

★
Evidence relating CYP1B1 rs1800440 G allele with increased levels of oestrogen metabolites

★★
Evidence relating CYP1B1 rs1800440 G allele with increased risk for endometriosis

★★
Evidence relating CYP1B1 rs1800440 G allele with increased risk for higher PAH metabolites

What do your results mean?

The AA genotype is associated with normal enzyme activity, and possibly lower levels of reactive metabolites, compared to those with the G allele.

Phase 1 Detox-related Genes > CYP1B1

Gene	Gene variation	rs number	Result	Effect
CYP1B1	C1294G/V432L	rs1056836	CG - +	

Legend

- No effect
- Pay attention
- Pay close attention
- - - Wild type
- - + Heterozygous
- + + Homozygous

Gene description

Cytochrome P450 enzyme 1B1 (CYP1B1) metabolises oestrone (E1) and oestradiol (E2) into the reactive 4-hydroxy metabolites, 4OH-E1 and 4OH-E2. CYP1B1 also metabolises environmental pollutants including polycyclic aromatic hydrocarbons (PAHs), which are released from burnt substances such as cigarette smoke, petroleum-related compounds and chargrilled meats. Genetic variations that increase enzyme activity may increase the amount of toxic and reactive metabolites that can impact both men and women's health. Individuals who inherit genetic variations within CYP1B1, that increase enzyme activity, should review the other hormone-related genes such as CYP17A1, CYP19A1, MTHFR and COMT, and/or CYP1A1 which also metabolises PAHs.

Level of evidence star rating

★★
Evidence relating CYP1B1 rs1056836 G allele and increased risk for endometriosis

★★
Evidence relating CYP1B1 rs1056836 G allele and reduced risk of benzene toxicity

★★
Evidence relating CYP1B1 rs1056836 GG genotype and improved semen parameters

★★★
Evidence relating CYP1B1 rs1056836 GG genotype and increased enzyme activity

What do your results mean?

The G allele has been associated with increased enzyme activity and may lead to reduced oestroadiol and increased levels of reactive metabolites that can cause DNA damage. There is mixed evidence regarding the effects of the CG genotype, which may have a minimal impact compared to the GG genotype. The variation has been associated with reduced risk for benzene toxicity and uterine fibroids along with increased risk for endometriosis. Research also suggests an association with improved sperm quality semen parameters. Individuals who inherit the G allele may benefit from reduced exposure to xenoestrogens and environmental pollutants.

Phase 1 Detox-related Genes > CYP2D6

Gene	Gene variation	rs number	Result	Effect
CYP2D6	*10 *4	rs1065852 rs3892097	*1/*1 - -	

Legend

- No effect
- Pay attention
- Pay close attention
- - - Wild type
- - + Heterozygous
- + + Homozygous

Gene description

The cytochrome P450 2D6 (CYP2D6) gene codes for an enzyme involved in the metabolism of over 25% of all clinically used medicines. Common examples include opioids, beta-blockers, antidepressants, anti-psychotics and tamoxifen. CYP2D6 is also involved in the synthesis of dopamine and serotonin. Genetic variations in CYP2D6 can result in reduced enzyme activity and loss of function. A large number of genetic variations have been identified in CYP2D6, with CYP2D6*4 (rs3892097) and CYP2D6*10 (rs1065852) being the most frequent across populations. The frequencies of CYP2D6*4 and *10 alleles differ greatly among ethnic groups. Approximately 25% of European Caucasians carry the CYP2D6*4 non-functional variant allele, but it is less frequent in African-Americans and is rarely detected in Asian populations. However, the CYP2D6*10 reduced function variant allele is present in approximately 40% of Asians compared to 3-10% in Africans and less than 2% in the European-Caucasian, resulting in a large proportion of slow-metaboliser phenotype (approximately 60% of normal activity). Africans frequently harbour duplications, which results in an ultra-rapid metaboliser phenotype causing increased risk of drug toxicity (e.g. symptoms of a morphine overdose following a standard dose of codeine). It has been speculated that the ultrarapid metaboliser was required for the detoxification of poisonous berries and therefore survival in African populations. This test does not detect duplications, nor other variations that may impact on enzyme activity. To determine an individual's ability to metabolise medications and make recommendations, more in depth pharmacogenomic testing is recommended. Please note, the star-allele nomenclature is a result of efforts to standardise pharmacogenomic testing. Key: *1/*1 = wild type; normal enzyme function *1/*4 = mild decrease in enzyme activity *1/*10 = reduced enzyme activity; classified as intermediate metaboliser *4/*4 = reduced enzyme activity; classified as poor metaboliser *4/*10 = reduced enzyme activity; classifies as intermediate metaboliser *10/*10 = reduced enzyme activity; classified as intermediate metaboliser *5/*5 = gene deletion; classified as poor metaboliser

What do your results mean?

The *1/*1 genotype (homozygous, wild-type alleles) is associated with normal enzyme function. Individuals with this genotype are classified as extensive metabolisers.

Phase 1 Detox-related Genes > CYP2C19

Gene	Gene variation	rs number	Result	Effect
CYP2C19	*17	rs12248560	*1/*1 - -	

Legend

- No effect
- Pay attention
- Pay close attention

- - Wild type
- - + Heterozygous
- + + Homozygous

Gene description

The cytochrome P450 2C19 (CYP2C19) gene codes for an enzyme that plays a role in the metabolism of at least 10% of commonly prescribed drugs. Substrates include proton pump inhibitors, anti-epileptics, warfarin and clopidogrel (an antiplatelet drug). CYP2C19 converts clopidogrel to its active form, which is necessary for the drug to function in the body. A genetic variation in CYP2D19 (rs12248560) results in an increased metabolic capacity of the CYP2C19 enzyme, which may alter drug clearance or activation rate. The variant allele frequency of this genetic variation (CYP2C19*17) shows ethnic variability with the variant allele most frequently identified in Europe and Middle-East regions (approximately 25%) but at a very low frequency in Asia (less than 2%). In addition, the frequency of CYP2C19*17 is particularly high in South-Europeans (42%). Approximately one third of Caucasians and Middle-Easterners are believed to display the (ultra)rapid metaboliser phenotype associated with this variant allele. CYP2C19 activity can be modulated by clinical as well as herbal medication. Low-dose aspirin (50mg/day) has been shown to significantly induce CYP2C19 enzyme activity, whereas St John's wort and gingko have been identified as CYP2C19 modulating herbs. Gingko biloba leaf extract of doses higher than the recommended 240mg/day can cause a mild induction in CYP219 enzyme activity. A dose of 900mg St John's wort per day can induce CYP2C19, irrespective of any genetic variation in CYP2C19 carried. To determine an individual's ability to metabolise medications and make recommendations more in depth pharmacogenomic testing is recommended, particularly for Asians who often have different CYP2C19 genetic variations.

Level of evidence star rating

★★★
Evidence relating the *1/*17 classification as rapid metabolizers

★★★
Evidence relating the *17 / *17 classification as ultra rapid metabolizers

What do your results mean?

The *1/*1 (CC genotype) is associated with normal enzyme function. Those with the *1/*1 genotype are classified as normal metabolisers.

Phase 1 Detox-related Genes > CYP3A4*1B

Gene	Gene variation	rs number	Result	Effect
CYP3A4*1B	-392A>G	rs2740574	AA - -	

Gene description

The CYP3A4 gene encodes the cytochrome P450 3A4 enzyme. CYP3A4 is predominantly expressed in the (adult) liver and small intestine and is involved in steroid metabolism, the oxidation of oestrogen, and the metabolism of at least half of the clinical drugs used today, including codeine, diazepam, erythromycin, acetaminophen, and cyclosporin. There is a high inter-individual variation in hepatic CYP3A4 with expression ranging up to 100-fold, which can markedly influence the disposition of drugs for which elimination is dependent on this enzyme. Furthermore, many medicines can CYP3A4 are potent inducers of CYP3A4, such as phenorbarbital, phenytoin, rifampicin, and many glucocorticoids. Environmental toxins (such as organochlorine pestides), diet (such as the principal ingredient of hot red and chilli peppers, capsaicin), and herbal medicine (such as St John's wort) have also been indicated to induce CYP3A4. In contrast, research has shown that grapefruit juice (and most likely also bitter orange, pomelo, and lime juice) is a potent inhibitor of intestinal CYP3A4, which may result in drug overdose toxicity. Star fruit and herbal/complementary medicine, such as goldenseal, schisandra, gingko biloba and black pepper (piperine or piperamides) supplements, may also reduce CYP3A4 efficacy. It is therefore recommended that healthcare professionals should ask patients about their dietary habits and use of alternative and complementary medicine, when considering medication that is metabolised by CYP3A4 to avoid potential diet-drug interactions. A genetic variation in CYP3A4, rs2740574, has been suggested to cause a mild change in enzyme activity; however, it is believed to be not of significant magnitude to have a clinical significant influence on drug metabolism. Africans and African-Americans are frequent carriers (65-80%) of the variant allele, CYP3A4*1B, whereas the allele is less common in Caucasians, Hispanics, and Asians (<10%).

What do your results mean?

Current data does not support an association of these genotypes with altered risks of adverse health outcomes or changes in detoxification reactions.

Legend

- No effect
- Pay attention
- Pay close attention

- - Wild type
- - + Heterozygous
- + + Homozygous

Phase 2 Detox-related Genes > NAT2

Gene	Gene variation	rs number	Result	Effect
NAT2	Paired SNP T>C Paired SNP C>T	rs1801280 rs1041983	RS - +	

Legend

- No effect
- Pay attention
- Pay close attention

- - Wild type
- - + Heterozygous
- + + Homozygous

Gene description

N-acetyltransferase 2 (NAT2) codes for a phase 2 detoxification enzyme that catalyses the acetylation of various chemicals present in the diet, environment and pharmaceuticals medications. Acetylation involves the conjugation of compounds with acetyl-coenzyme A making them less reactive and easy to excrete. Acetylation is the major degradation pathway for aromatic amines (arylamines) and hydrazines, which are found in caffeine, meat and fish cooked at high temperatures, as well as in combustion smoke such as those found in tobacco and exhaust fumes. NAT2 is found predominantly in the liver and the gut. Individuals acetylate, and therefore detoxify toxins and chemicals, at different rates. They can be described as slow (SS), intermediate (RS or SR) or rapid (RR) acetylators based on several genetic variations within NAT2. Individuals who are slow acetylators may be more chemically sensitive because reduced NAT2 enzyme activity may prolong the action of chemicals and pharmaceutical medications, thus enhancing toxicity. Slow acetylation has been associated with increased risk for oxidative stress, DNA damage and may play a role in adverse health conditions such as endometriosis. It is important to note that rapid acetylators can add acetyl groups so quickly that mistakes may occur, resulting in some toxins becoming more reactive; this is of particular concern when exposed to a high toxic load. To determine if an individual is a slow, intermediate or rapid acetylator genetic variations referred to as a tag and paired SNP combinations are reported that classify 96% of the Caucasian, East and South Asian population. RR = rapid RS and SR = intermediate SS = slow

What do your results mean?

The RS genotype is associated with intermediate enzyme activity (intermediate acetylator), resulting in intermediate detoxification of particular chemicals. This comes from a paired SNP and represents multiple genetic variations within NAT2.

Phase 2 Detox-related Genes > NAT2

Gene	Gene variation	rs number	Result	Effect
NAT2	Tag SNP G>A	rs1495741	GA - +	

Legend

- No effect
- Pay attention
- Pay close attention

- - Wild type
- - + Heterozygous
- + + Homozygous

Gene description

N-acetyltransferase 2 (NAT2) codes for a phase 2 detoxification enzyme that catalyses the acetylation of various chemicals present in the diet, environment and pharmaceuticals medications. Acetylation involves the conjugation of compounds with acetyl-coenzyme A making them less reactive and easy to excrete. Acetylation is the major degradation pathway for aromatic amines (arylamines) and hydrazines, which are found in caffeine, meat and fish cooked at high temperatures, as well as in combustion smoke such as those found in tobacco and exhaust fumes. NAT2 is found predominantly in the liver and the gut. Individuals acetylate, and therefore detoxify toxins and chemicals, at different rates. They can be described as slow (SS), intermediate (RS or SR) or rapid (RR) acetylators based on several genetic variations within NAT2. Individuals who are slow acetylators may be more chemically sensitive because reduced NAT2 enzyme activity may prolong the action of chemicals and pharmaceutical medications, thus enhancing toxicity. Slow acetylation has been associated with increased risk for oxidative stress, DNA damage and may play a role in adverse health conditions such as endometriosis. It is important to note that rapid acetylators can add acetyl groups so quickly that mistakes may occur, resulting in some toxins becoming more reactive; this is of particular concern when exposed to a high toxic load. To determine if an individual is a slow, intermediate or rapid acetylator genetic variations referred to as a tag and paired SNP combinations are reported that classify 96% of the Caucasian, East and South Asian population. RR = rapid RS and SR = intermediate SS = slow

Level of evidence star rating

★★
Evidence relating the slow phenotype with increased oxidative stress

★★★
Evidence relating the slow phenotype with phase II detoxification/slow acetylation of particular chemicals

★★★★
Evidence relating to enzyme activity (rapid, intermediate, slow)

What do your results mean?

The GA genotype is associated with intermediate enzyme activity (intermediate acetylator) resulting in intermediate detoxification of particular chemicals. This genetic variation is referred to as a tag SNP, meaning it is a marker for multiple genetic variations within NAT2.

Phase 2 Detox-related Genes > GSTP1

Gene	Gene variation	rs number	Result		Effect
GSTP1	A313G	rs1695	AA	- -	

Legend

- No effect
- Pay attention
- Pay close attention
- - - Wild type
- - + Heterozygous
- + + Homozygous

Gene description

Glutathione S-transferase P1 (GSTP1) is a phase 2 detoxification enzyme. GSTP1 conjugates glutathione to reactive metabolites and xenobiotics, converting them to less reactive substances in order to be excreted from the body. Glutathione S-transferases (GSTs) are a family of enzymes that play a significant role in the detoxification of many potentially harmful substances, with the addition of reduced glutathione. GSTs also play a role in the conjugation of catechol oestrogens and their oxidative metabolites. GSTs are categorised into four main classes: alpha (A), mu (M), pi (P) and theta (T). Unlike other GSTs that are mainly expressed in the liver, GSTP1 is predominantly expressed in the lungs, brain, breast and placenta. The GSTP1 enzyme activity is substrate dependant. Therefore the influence on an individual's health may depend on the specific reactive metabolite that needs to detoxified and excreted. GST activity is dependent on glutathione availability, exposures and overall functionality of GSTs. Individuals who inherit genetic variations within GSTP1 that reduce enzyme activity should review the other antioxidant and detoxification related genes such as CYP1B1, MnSOD and CAT to help determine susceptibility.

Level of evidence star rating

★★
Evidence or nutrient inducers

★★
Evidence relating the GSTP1 rs1695 G allele and increased DNA damage (PAH DNA adducts)

★★★
Evidence relating the GSTP1 rs1695 G allele and reduced enzyme activity

What do your results mean?

The AA genotype is associated with normal enzyme activity.

Phase 2 Detox-related Genes > GSTP1

Gene	Gene variation	rs number	Result		Effect
GSTP1	C341T	rs1138272	CC	- -	

Legend

- No effect
- Pay attention
- Pay close attention
- - - Wild type
- - + Heterozygous
- + + Homozygous

Gene description

Glutathione S-transferase P1 (GSTP1) is a phase 2 detoxification enzyme. GSTP1 conjugates glutathione to reactive metabolites and xenobiotics, converting them to less reactive substances in order to be excreted from the body. Glutathione S-transferases (GSTs) are a family of enzymes that play a significant role in the detoxification of many potentially harmful substances, with the addition of reduced glutathione. GSTs also play a role in the conjugation of catechol oestrogens and their oxidative metabolites. GSTs are categorised into four main classes: alpha (A), mu (M), pi (P) and theta (T). Unlike other GSTs that are mainly expressed in the liver, GSTP1 is predominantly expressed in the lungs, brain, breast and placenta. The GSTP1 enzyme activity is substrate dependant. Therefore the influence on an individual's health may depend on the specific reactive metabolite that needs to detoxified and excreted. GST activity is dependent on glutathione availability, exposures and overall functionality of GSTs. Individuals who inherit genetic variations within GSTP1 that reduce enzyme activity should review the other antioxidant and detoxification related genes such as CYP1B1, MnSOD and CAT to help determine susceptibility.

Level of evidence star rating

★★
Evidence or nutrient inducers

★★
Evidence relating the GSTP1 rs1138272 T allele and reduced enzyme activity

What do your results mean?

The CC genotype is associated normal enzyme activity.

Phase 2 Detox-related Genes > NQO1

Gene	Gene variation	rs number	Result	Effect
NQO1	C609T	rs1800566	CT - +	

Legend

- No effect
- Pay attention
- Pay close attention

- - Wild type
- - + Heterozygous
- + + Homozygous

Gene description

Quinone oxidoreductase 1 (NQO1), referred to as quinone reductase, codes for an enzyme that acts as an antioxidant in the detoxification of reactive and harmful quinones. NQO1 converts ubiquinone, the inactive form of CoQ10, into the the active form ubiquinol and vitamin E alpha-tocopherol quinone into the active form alpha-tocopherol. Therefore, NQO1 helps to protect cells from oxidative stress by maintaining the antioxidant forms of CoQ10 and vitamin E. In addition, NQO1 converts reactive and potentially harmful quinones derived from benzenes, nitrogen dioxide, tobacco smoke and oestrogen metabolites into less harmful substances. Studies of NQO1 rs1800566 indicate the variation has a marked impact on the protein and enzyme activity, resulting in increased reactive quinones, oxidative stress and risk for various adverse health conditions. Vitamin B2 is required for flavin adenine dinucleotide (FAD), the cofactor for NQO1. Individuals who inherit genetic variations within NQO1 that reduce enzyme activity should review the other antioxidant and detoxification related genes such as MnSOD, GPX1, CAT, CYPs and GSTP1 to help determine individual susceptibility.

Level of evidence star rating

★★★
Evidence relating the T allele and increased risk for benzene toxicity

★★★
Evidence relating the T allele and reduced enzyme activity

★★★
Evidence relating the T allele with reduced quinone/catechol detoxification

What do your results mean?

The T allele significantly reduces NQO1 enzyme activity. Research indicates the TT genotype is associated with total loss of function and the CT genotype is associated with greatly reduced enzyme activity. The T allele results in reduced ability to maintain the antioxidant forms of CoQ10 and vitamin E, and the reduced ability to detoxify reactive quinone compounds such as catechol quinones. The T allele has been associated with increased risk for benzene toxicity. If supplementation is required, the individual may benefit from ubiquinol rather than ubiquinone.

Phase 2 Detox-related Genes > COMT

Gene	Gene variation	rs number	Result	Effect
COMT	G158A	rs4680	GA - +	

Legend

No effect

Pay attention

Pay close attention

- - Wild type

- + Heterozygous

+ + Homozygous

Gene description

This gene codes for the catechol-o-methyl transferase (COMT) enzyme. COMT transfers a methyl group from S-adenosylmethionine (SAMe) to catecholamines, using magnesium as a cofactor. This enzyme metabolises/inactivates catecholamines, including the neurotransmitters dopamine, adrenalin, noradrenalin, as well as catechol oestrogens. Altered enzyme activity may lead to changes in active amounts of neurotransmitters, OH-oestrogen metabolites and other catechol compounds. COMT may also be important for the metabolism of catechol drugs.

Level of evidence star rating

★
Evidence relating the A allele and oestrogen metabolites

★★
Evidence relating the A allele and increased cognitive function

★★
Evidence relating the A allele and increased risk for anxiety

★★
Evidence relating the A allele and pain sensitivity

★★★
The A allele is associated with reduced MTHFD1 enzyme activity

What do your results mean?

The GA (Val/Met) allele is associated with reduced COMT activity, therefore reduced methylation and breakdown of catecholamines and catechol oestrogens, which may result in higher levels of 4-OH oestrogens and catecolamines such as dopamine and adrenalin. Increased 4-OH oestrogens can become oxidised to catechol quinones and can increase the risk for DNA damage. In addition, higher levels of neurotransmitters, such as adrenalin, may influence stress, anxiety and pain sensitivity.

Antioxidants > SOD2

Gene	Gene variation	rs number	Result	Effect
SOD2	C47T	rs4880	CC - -	

Legend

- No effect
- Pay attention
- Pay close attention

- - Wild type
- - + Heterozygous
- + + Homozygous

Gene description

Manganese superoxide dismutase (MnSOD) codes for a key antioxidant enzyme that converts harmful reactive oxygen species (ROS) to less harmful metabolites in order to protect cells from ROS induced damage (oxidative stress). MnSOD requires manganese as a cofactor and is also known as SOD2. MnSOD is the only known antioxidant enzyme present in the mitochondria. Specifically, the enzyme breaks down the free radical superoxide into hydrogen peroxide, which in-turn is neutralised to water and oxygen by catalase (CAT) or glutathione peroxidase (GPX). MnSOD, together with CAT and GPX, make up the body's primary defense system that break down excess ROS in order to maintain the balance between antioxidant activity and oxidative stress. MnSOD enzyme activity is dependent on manganese availability, exposures and ROS levels. Individuals who inherit genetic variations within MnSOD that reduce enzyme activity should review the other antioxidant and detoxification related genes such as GPX1, CAT and GSTP1 to help determine individual susceptibility.

Level of evidence star rating

★★
Evidence relating the T allele and increased risk for endometriosis

★★
Evidence relating the T allele with reduced enzyme activity and increased risk for oxidative stress

★★
Evidence relating to T allele and increased sperm DNA damage

What do your results mean?

The CC genotype is associated with normal antioxidant enzyme activity.

Antioxidants > GPX1

Gene	Gene variation	rs number	Result		Effect
GPX1	linkage with rs1050450	rs1800668	CC	- -	

Legend

- No effect
- Pay attention
- Pay close attention

- - Wild type
- - + Heterozygous
- + + Homozygous

Gene description

GPX1 rs1800668 (in linkage with rs1050450) The glutathione peroxidase 1 (GPX1) gene codes for a selenium-dependent antioxidant enzyme. GPX1 breaks down hydrogen peroxide and organic hydroperoxides with glutathione into water and oxygen in order to prevent oxidative damage to cells. GPX1 is the most abundant form of glutathione peroxidase found in cells and is expressed in the cytoplasm. GPX1, together with manganese superoxide dismutase (MnSOD) and catalase (CAT), make up the body's primary defense system that break down excess reactive oxygen species (ROS) such as hydrogen peroxide, thereby maintaining the balance between oxidative stress and antioxidant activity. Oxidative stress is hypothesised to play a role in the development of pregnancy complications, autoimmune disorders and age-related diseases. A genetic variation within the GPX1 gene rs1800668 is linked with another variation rs1050450, meaning the two variations are likely to be inherited together. Evidence suggests these variations are associated with reduced antioxidant enzyme activity, which may result in increased risk for high oxidative stress.

Level of evidence star rating

★★
Evidence relating the T allele with reduced anti-oxidant enzyme activity

★★
Evidence that a selenium can increase glutathione peroxidase (GPX) activity

What do your results mean?

The CC genotype is associated with normal antioxidant enzyme activity.

Antioxidants > CAT

Gene	Gene variation	rs number	Result	Effect
CAT	C-262T	rs1001179	CT - +	

Legend

- No effect
- Pay attention
- Pay close attention

- - Wild type
- - + Heterozygous
- + + Homozygous

Gene description

The catalase (CAT) gene codes for a haem-containing antioxidant enzyme that is required to break down reactive oxygen species (ROS), also known as free radicals, that can damage cells and tissues. Specifically, CAT breaks down hydrogen peroxide (H2O2) into water (H2O) and oxygen (O2). CAT is found in various cells and tissues throughout the body but is most abundant in the liver (peroxisomes in hepatocytes), kidney and erythrocytes (cytoplasm). CAT, together with manganese superoxide (MnSOD) and glutathione peroxidise (GPX), make up the body's primary defense system that break down excess ROS and thereby maintains the balance between oxidative and antioxidative activity. Oxidative stress is hypothesised to play a role in the development of pregnancy and autoimmune disorders as well as chronic and late-onset diseases. A genetic variation within the CAT gene (rs1001179) is associated with reduced antioxidant enzyme activity, which may result in reduced antioxidant protection against oxidative stress. Research suggests that the effect of the CAT genetic variation on enzyme activity may differ among ethnicities, with altered activity observed in individuals of Caucasian descent but not in those of African-American descent. Environmental exposure to high levels of ROS, such as frequent exposure to fine dust or over training (high intensity and high frequency exercise), may also reduce catalase activity in T allele carriers and thereby negatively impact adverse health outcomes.

Level of evidence star rating

★★
Evidence relating the T allele and reduced enzyme activity

What do your results mean?

The T allele is associated with reduced antioxidant enzyme activity and may increase the risk for oxidative stress. Individuals who inherit the CT genotype have a approximately 18% less antioxidant enzyme activity and those with the TT genotype have approximately 33% less antioxidant enzyme activity, compared to the CC genotype. A dietary intake rich in antioxidants (e.g. high in fruits and vegetables) is associated with reduced catalase activity in T allele carriers, which is most likely due to the antioxidant capacity of fruits and vegetables reducing the oxidative burden. Regular physical activity has been shown to enhance total antioxidant capacity and may render cells more resistant to oxidative stress.

Antioxidants > PON1

Gene	Gene variation	rs number	Result	Effect
PON1	Q192R	rs662	AG - +	

Legend

- No effect
- Pay attention
- Pay close attention

- - Wild type
- - + Heterozygous
- + + Homozygous

Gene description

The paraoxonase 1 (PON1) gene codes for a calcium-dependent enzyme that breaks down a variety of compounds, including organophosphates, nerve gases, glucuronide drugs, cyclic carbamates, thiolactones and oestrogen esters. PON1 collaborates with apolipoprotein A1 (APOA1) and high-density lipoproteins (HDLs) to help prevent low-density lipoprotein (LDL) oxidation. PON1 also breaks down homocyseine-thiolactone helping to reduce homocysteine mediated oxidative stress and protein damage. PON1 activity is very low at birth and increases over time, reaching adult levels between 6 months and 2 years of age. Low paraoxonase activity has been associated with increased oxidative stress and may increase susceptibility to plaque formation, atherosclerosis and cardiovascular disease, as well as adverse health effects as a result of organophosphate exposure. Increased PON1 activity has been observed following vitamin C, vitamin E, folate, carotenoids, mono and polyunsaturated fatty acids, selenium and polyphenols supplementation. A genetic variation in PON1 (rs662) has been shown to affect enzyme activity in a substrate-specific manner. Wild-type allele carriers are more efficient in preventing LDL oxidation and detoxifying the organophosphates sarin, diazoxon and soman compared to variant allele carriers. In contrast, those with the variant allele show increased PON1 activity for converting homocyseine-thiolactone into homocysteine and an increased ability to break down paraoxon, methylparaoxon, armin, chlorthion oxon and EPN oxon compared to wild-type carriers. Whereas enzyme activity was shown to be comparable in wild-type and variant allele carriers for phenyl acetate and 2-naphtyl acetate. Variant allele carriers are also more sensitive to enzyme inhibition by cadmium, zinc, mercury chloride and iron, whereas wild-type allele carriers display increased inhibition in response to lead.

Level of evidence star rating

★★
Evidence relating to altered enzyme activity (substrate specific)

★★★
Evidence relating to detoxification and oxidative stress levels

What do your results mean?

The AG genotype is associated with increased LDL oxidation compared to the AA genotype and therefore may the increase risk of atherosclerosis and cardiovascular disease. In regards to organophosphate exposure, the AG genotype shows a moderately increased ability to break down paraoxon, chlorpyrifos, methylparaoxon, armin, chlorthion oxon, EPN oxon, but a moderately reduced ability to metabolise sarin, diazoxon and soman compared to the AA genotype. Therefore, the AG genotype carriers exhibit a moderate reduced and a moderate increased risk of adverse health effects depending on the type of organophosphate exposure.

Neurotransmitters And Mood > MAO-A

Gene	Gene variation	rs number	Result	Effect
MAO-A	X-chr	rs909525	AA - -	

Legend

- No effect
- Pay attention
- Pay close attention

- - Wild type
- - + Heterozygous
- + + Homozygous

Gene description

The monoamine oxidase A (MAO-A) gene codes for an enzyme that metabolises the neurotransmitters dopamine, serotonin, adrenaline, noradrenaline as well as xenobiotic amines. Specifically, MAO-A catalyses the oxidative deamination (breakdown) of amines. Therefore, MAO-A activity is important for regulating the balance of catecholamine neurotransmitters and may influence mood and behaviour. During the breakdown of these amines, hydrogen peroxide, aldehydes and ammonia are produced. Research indicates MAO-A expression is influenced by gender, previous trauma and genetic variations that alter enzyme activity. The genetic variation rs909525 has been shown to alter gene expression. The AA or TT genotype increases expression and is referred to as high activity or 4-5R; the GG or CC genotype reduces expression and is referred to as low activity or 2-3R. The R stands for repeat, which impacts on transcription and expression. An increase in repeats results in increased transcription, and therefore increased expression and MAO-A protein levels. This particular variation is often shown with different alleles depending on the DNA strand tested. The reverse (minus) strand gives the result A/G; the forward (plus) strand gives the result T/C. MAO-A is commonly referred to as a ‘warrior’ gene. It is located on the X chromosome and is found in the liver, kidney, intestine and brain.

Level of evidence star rating

★★
Evidence relating the AA genotype increased MAOA activity

★★
Evidence relating the GG genotype with decreased MAOA activity and increased aggression (note studies indicate this is dependent on environmental interactions)

What do your results mean?

The AA genotype is associated with high MAO-A activity (4-5R). High MAO-A activity is associated with reduced levels of neurotransmitters in the brain, such as serotonin. Individuals who inherit this genotype are less likely to be aggressive and less prone to alcoholism compared to the GG genotype. The AA genotype may be associated with anxiety, low mood and some mood disorders. The A allele is considered the "non-warrior" allele. These results are also influenced by gender and environment, with males being more susceptible to these outcomes.

Neurotransmitters And Mood > DRD2/ANNK1

Gene	Gene variation	rs number	Result	Effect
DRD2/ANNK1	Taq1a	rs1800497	CC - -	

Legend

- No effect
- Pay attention
- Pay close attention
- - - Wild type
- - + Heterozygous
- + + Homozygous

Gene description

The dopamine receptor D2 (DRD2) gene codes for a receptor that binds to dopamine in the brain. DRD2 is highly expressed in regions of the brain closely associated with the motor and reward systems. DRD2 is involved in various functions including learning, memory, attention, reward behaviour and regulation of movement. Dopamine receptors are present in the cerebral arteries that are believed to be involved in the pathogenesis of a migraine. The DRD2/ANNK1 receptor antagonists have been proposed as anti-migraine medication. A role of the dopaminergic system in the pathophysiology of migraines has been suggested, as the dopaminergic system is responsible for maintaining the dopamine:norepinephrine ratio. Imbalances in this ratio make individuals susceptible to a migraine. In those who suffer migraines, the level of plasma norepinephrine is significantly lower compared with controls, indicating a sympathetic dysfunction. A genetic variation (rs1800497), known as the Taq1A polymorphism, is associated with differences in the number of DRD2 receptors in the brain and may increase the risk for addictive behaviours such as alcoholism, smoking and opioid dependence. There have been mixed reports on the direct effect of rs1800497 and dopamine on eating behaviour and obesity. However, in those who are already obese, it is possible that carrying the rs1800497 T (A1) allele may be a risk factor for putting on more weight, which may be linked to psychological reasons. Please note, the rs1800497 genetic variation was initially reported to be in the DRD2 gene. However, further investigations determined the variation is 10,000 base pairs down from the gene and located within the ANNK1 gene. Regardless of location, studies show that the genetic variant rs1800497 is significantly associated with dopamine receptor binding potential. It is possible that rs1800497 is in linkage (inherited along with) a genetic variant within DRD2 that is the causal variant.

Level of evidence star rating

★★
Evidence relating the T allele and addictive behaviours Â

★★★★
Evidence relating the T allele with a reduced number of DRD2 receptors and reduced binding potential

What do your results mean?

The CC genotype is associated with normal DRD2 receptor activity and does not alter learning, memory, behaviour or susceptibility to migraines.

Neurotransmitters And Mood > TH

Gene	Gene variation	rs number	Result	Effect
TH	C824T	rs10770141	CT - +	

Gene description

Tyrosine hydroxylase (TH) codes for an enzyme that converts L-tyrosine into L-DOPA. L-DOPA is the precursor for dopamine, which in-turn can be converted into noradrenalin and adrenalin. Therefore, TH is considered the rate-limiting enzyme in the synthesis of catecholamines including dopamine, noradrenalin and adrenalin. TH enzyme activity is dependent on tetrahydrobiopterin (BH4) and the cofactor iron. TH is expressed in the central nervous system, peripheral sympathetic neurons and the adrenal medulla. A genetic variation within TH (rs10770141) is reported to influence catecholamine levels and may impact on blood pressure, perceived stress and anxiety. In addition, environmental factors, such as alcohol, can impact TH expression. Acute alcohol exposure can cause an increase in TH and dopamine synthesis, however chronic exposure may result in decreased TH levels and reduced dopamine.

Level of evidence star rating

★★
Evidence relating the T allele with stress-induced high blood pressure and hypertension

★★★
Evidence relating the T allele with increased transcription and levels of catecholamines

What do your results mean?

The T allele is associated with increased enzyme activity and increased levels of catecholamines. In addition, the T allele is associated with stress-induced hypertension. Increased catecholamines may increase the risk for stress and anxiety.

Legend

- No effect
- Pay attention
- Pay close attention

- - Wild type
- - + Heterozygous
- + + Homozygous

Neurotransmitters And Mood > DAO

Gene	Gene variation	rs number	Result	Effect
DAO	C47T	rs10156191	CT - +	

Legend

- No effect
- Pay attention
- Pay close attention

- - Wild type
- - + Heterozygous
- + + Homozygous

Gene description

The gene known as diamine oxidase (DAO) also known as Amine oxidase (AOC1) codes for an enzyme involved in the degradation of histamine and is involved in allergic and immune responses along with cell proliferation and tissue differentiation. Histamine is released by cells in response to injury and allergic reactions. Histamine is involved in the inflammatory response, and mediates itching and changes in blood vessels to allow immune cells and proteins in to infected tissues. Histamine also acts as a neurotransmitter for the brain, spinal cord and uterus. Abnormal histamine is associated with inflammation in the brain, migraines and neurological conditions. DAO is an enzyme dependant on flavin adenine dinucleotide (FAD), vitamin B2 and copper. Genetic variants within DAO are associated with reduced DAO activity, which in-turn may decrease the ability to break down histamine. DAO variants are not associated with histamine intolerance in isolation. Research indicates histamine intolerance is caused by an interaction between genetic and environmental factors.

Level of evidence star rating

★★
Evidence relating the T allele and decreased enzyme activity

★★
Evidence relating the T allele and increased sensitivity to NSAID's and salicylic acid

What do your results mean?

The T allele is associated with reduced DAO enzyme activity. Individuals who inherit the CT genotype are more susceptible to migraines.

Neurotransmitters And Mood > GAD1

Gene	Gene variation	rs number	Result	Effect
GAD1	147G>A	rs3749034	GG - -	

Legend

- No effect
- Pay attention
- Pay close attention

- - Wild type
- - + Heterozygous
- + + Homozygous

Gene description

The glutamic acid decarboxylase 1 gene (GAD1) codes for a vitamin B6-dependent enzyme that converts glutamate, an excitatory neurotransmitter, into gamma-aminobutyric acid (GABA), an inhibitory neurotransmitter. GABA is the most abundant inhibitory neurotransmitter in the central nervous system and is found in various regions of the brain, including the hypothalamus and cerebellum, where it is involved in motor function. GABA reduces the activity of neurons and is thought to help reduce fear and anxiety experienced when neurons are overexcited. GAD is also expressed in the pancreas and and has been identified as a major autoantigen in insulin-dependent diabetes. Research shows that GAD1, and ultimately GABA, may be involved in working memory, panic disorder and a number of other mood related disorders. Animal studies suggest that oestrogen and progesterone decrease GAD expression, which theoretically provides a link between hormone levels, anxiety and mood disorders in women. Benzodiazepines are pharmaceuticals used to treat anxiety and mood disorders that cause an increase in the responsiveness of the GABA receptor.

Level of evidence star rating

★★
Evidence relating the A allele with lower GAD1 transcription

★★
Evidence relating the A allele with poorer working memory and mood disorders

What do your results mean?

The GG genotype is associated with normal enzyme activity.

Neurotransmitters And Mood > BDNF

Gene	Gene variation	rs number	Result		Effect
BDNF	Val66Met	rs6265	GG	- -	

Legend

- No effect
- Pay attention
- Pay close attention
- - - Wild type
- - + Heterozygous
- + + Homozygous

Gene description

The BDNF gene codes for brain-derived neurotrophic factor (BDNF). BDNF belongs to a family of neurotrophins, which are proteins essential for the development, survival and function of neurons. In early life, BDNF is involved in neurogenesis and neurodevelopment. Whereas, later in life, it facilitates the strengthening of nerve pathways, neuronal plasticity and neuroprotection. BDNF is expressed throughout the central and peripheral nervous system and impacts on many downstream pathways. It is associated with learning, memory, behaviour, stress, pain and energy metabolism. Furthermore, BDNF has been linked with eating disorders and body weight. BDNF has been shown to induce excitatory (glutamatergic) synapses and weaken inhibitory (GABAergic) synapses. Research suggests effective antidepressants increase BDNF, therefore BDNF may mediate the therapeutic actions of antidepressants. Higher levels of BDNF are associated with better working memory and lower BDNF is associated with an increased risk for mood disorders. The Val66Met variation within BDNF is associated with lower BDNF levels and reduced protein function. Exercise promotes the expression of BDNF, improving cognitive performance and helping alleviate depression and anxiety. Stress, on the other hand, can decrease BDNF levels and increase the risk for depression. Significantly lower levels of BDNF have been observed in migraine sufferers.

Level of evidence star rating

★★
Evidence relating the A allele with neurodegenerative disease

★★
Evidence relating the GG genotype with weight and obesity

★★★
Evidence relating the A alelle and mood disorders

★★★
Evidence relating the A allele and personality traits

What do your results mean?

The GG genotype is associated with better working memory and reduced risk of mood disorders and migraine compared to the AA genotype. However, individuals with the GG genotype may be at increased risk for overweight or obesity.

Blood Pressure > AGT

Gene	Gene variation	rs number	Result	Effect
AGT	T803C	rs699	TT - -	

Legend

- No effect
- Pay attention
- Pay close attention
- - - Wild type
- - + Heterozygous
- + + Homozygous

Gene description

The angiotensinogen gene (AGT) codes for the protein angiotensinogen, which is involved in regulating blood pressure and the balance of fluids and salts in the body. AGT is a precursor for angiotensin. Angiotensin causes increased blood pressure via multiple mechanisms including blood vessel constriction, increased sodium retention in the blood and increased sodium re-absorption in the kidneys. High blood pressure is associated with increased risk for cardiovascular disease and pregnancy complications such as gestational hypertension and preeclampsia. Genetic variations within the AGT gene are associated with susceptibility to high blood pressure (hypertension). Some studies suggest a genetic variation within AGT rs699 is associated with salt sensitivity, meaning individuals with the variant genotype keep more sodium in the blood. AGT levels are increased by corticosteroids, oestrogen and thyroid hormones.

Level of evidence star rating

★★
Evidence relating the C allele and hypertensive pregnancy complications

★★
Evidence relating the C allele with reduced salt intake

★★★
Evidence relating the C allele with increased angiotensin (AGT) and risk for high blood pressure Â

★★★
Evidence relating to exercise

What do your results mean?

The TT genotype is associated with normal AGT levels and reduced risk of high blood pressure compared to the CC genotype. Despite the lower risk genotype, it is important to note that blood pressure is significantly influenced by lifestyle factors including diet and exercise.

Blood Pressure > NOS3

Gene	Gene variation	rs number	Result	Effect
NOS3	G894T	rs1799983	GT - +	

Legend

- No effect
- Pay attention
- Pay close attention

- - Wild type
- - + Heterozygous
- + + Homozygous

Gene description

Endothelial nitric oxide synthase is an enzyme often referred to as nitric oxide synthase 3 (NOS3). Nitric oxide synthases are a family of enzymes that catalyse the production of nitric oxide (NO) from L-arginine. NOS3 provides continuous local production of NO in the vascular endothelium. NO acts as a potent vasodilator and is therefore essential for endothelial function, vascular tone and blood pressure. NO has diverse regulatory functions including smooth muscle relaxation, inhibition of platelet aggregation, immune regulation, neurotransmission and cellular proliferation. A common variant within NOS3 (rs1799983) is associated with altered enzyme activity and increased risk for hypertension, particularly in overweight individuals. Reduced production of NO is an important contributor to endothelial dysfunction, an underlying cause of various pregnancy and metabolic disorders as well as migraines. In addition, the NOS3 G894T genetic variation has been associated with homocysteine levels, which has been identified as a potential migraine risk factor.

Level of evidence star rating

★★
Evidence relating the T allele and reduced nitric oxide levels

★★★
Evidence relating the T allele altered enzyme activity

★★★
Evidence relating the T allele with hypertension

What do your results mean?

The NOS3 T allele results in an amino acid change from glutamic acid (Glu) to aspartic acid (Asp) at position 298 (Glu298Asp). The variation results in altered enzyme activity and may reduce NO production and endothelial-dependent vasodilation. The T allele, particularly the TT genotype, is associated with increased risk for hypertension and associated disorders, which may be compounded in those who are overweight. The GT genotype has not been associated with altered susceptibility to either a migraine with or without aura.

Clotting Factors > F2

Gene	Gene variation	rs number	Result	Effect
F2	G20210A	rs1799963	GG - -	

Legend

- No effect
- Pay attention
- Pay close attention

- - Wild type
- - + Heterozygous
- + + Homozygous

Gene description

The Factor II (F2) gene codes for a coagulation factor, prothrombin. Prothrombin is a vitamin K-dependent protein involved in in blood clotting, inflammation and blood homeostasis. Prothrombin is cleaved to form thrombin, which converts fibrinogen to fibrin for blood clot formation, platelet aggregation and activation of other coagulation factors. Prothrombin is produced in greater amounts after a blood vessel is damaged. This protein plays a role in maintaining vascular integrity during development and postnatal life. Prothrombin also produces peptides that have antimicrobial activity against Escherichia coli and Pseudomonas aeruginosa. A genetic variation (rs1799963), commonly known as the prothrombin G20210A mutation or the Factor II mutation, results in increased prothrombin and increased risk for inherited thrombophilia (clotting disorders). Clotting disorders are associated with various health conditions including cardiovascular and pregnancy complications. Due to the interactions of coagulation factors, it is advised to review the results for F2 and F5 together.

Level of evidence star rating

★★
Evidence relating the A allele and pregnancy complications

★★★★
Evidence relating the A allele with increased F2 (prothrombin) and increased risk for clotting

What do your results mean?

The GG genotype is associated with normal F2 (prothrombin) protein levels.

Clotting Factors > F5

Gene	Gene variation	rs number	Result	Effect
F5	G1601A	rs6025	GG - -	

Legend

- No effect
- Pay attention
- Pay close attention

- - Wild type
- - + Heterozygous
- + + Homozygous

Gene description

The Factor V (F5) gene codes for a coagulation factor called Factor V. Coagulation factors are essential for blood clotting and blood homeostasis. F5 is inactive until injury to a blood vessel triggers the activation via the coagulation system. Once activated, F5 is involved in the conversion of prothrombin (F2) to thrombin, which is required for blood clotting. A genetic variation (rs6025), commonly known as the Factor V Leiden, results in the increased risk for inherited thrombophilia (clotting disorders). Clotting disorders are associated with various health conditions including cardiovascular and pregnancy complications. Due to the interactions of coagulation factors it is advised to review the results for F2 and F5 together. It is important to note that many people with F5 and F2 variants do not develop blood clots. Blood clots usually develop when there are other risk factors such as long flights and being overweight/obese. However, if genetic variants are detected, it's important to see your doctor because blood clots can be life threatening if not treated early.

Level of evidence star rating

★★★
Evidence relating the A allele and pregnancy complications

★★★★
Evidence relating the A allele plus hormone/oestrogen therapy and risk for clotting

★★★★
Evidence relating the A allele with increased F5 level and increased risk for clotting

What do your results mean?

The GG genotype is associated with normal F5 protein levels, and reduced risk for blood clotting, compared to the GA and AA genotypes.

Hormone Receptor And Thyroid > LHCGR

Gene	Gene variation	rs number	Result	Effect
LHCGR	A226096G	rs13405728	AA - -	●

Legend

- ○ No effect
- ◐ Pay attention
- ● Pay close attention

- - - Wild type
- - + Heterozygous
- + + Homozygous

Gene description

Luteinising hormone choriogonadotropin receptor (LHCGR) codes for the receptor for both luteinising hormone (LH) and chorionic gonadotropin (CG). LHCGR is essential for foetal sex differentiation and adult reproductive function. In males, LHCGR is critical for testosterone production and supporting spermatogenesis. In females, LHCGR stimulates androgen production, providing the substrate for oestrogen to trigger puberty and support ovulation. In females, oestrogen, LH and follicle stimulating hormone (FSH) up-regulate LHCGR. A genetic variation within LHCGR (rs13405728) has been associated with increased risk for polycystic ovarian syndrome (PCOS) and ovulatory dysfunction.

Level of evidence star rating

★★
Evidence relating the A allele and increased risk for slow ovarian response in ART

★★
Evidence relating the A allele with increased risk for high glucose in PCOS women

★★★★
Evidence relating the A allele and increased risk for PCOS

What do your results mean?

The A allele is associated with an increased risk for PCOS and may effect ovulation and fertility. In addition, research suggests the AA genotype may be associated with slow ovarian response during assisted reproductive technology (ART) fertility treatment.

Hormone Receptor And Thyroid > PGR

Gene	Gene variation	rs number	Result	Effect
PGR		rs1042838	GT - +	

Legend

- No effect
- Pay attention
- Pay close attention

- - Wild type
- - + Heterozygous
- + + Homozygous

Gene description

This gene codes for the progesterone receptor (PGR), which mediates the physiological effects of the hormone progesterone. Progesterone stimulates and regulates various functions including the menstrual cycle, the establishment and maintenance of pregnancy and also plays a role in sexual desire. In addition, it is involved in the central nervous system, bone and cardiovascular health. Progesterone complements oestrogen and plays an important role with testosterone, as it is the precursor for adrenal hormones. Men produce a small amount of progesterone to aid in the development of sperm. High levels of progesterone are thought to be responsible for symptoms of premenstrual syndrome such as breast tenderness, bloating and mood swings. PGR is expressed in a variety of tissues including the uterus, mammary gland, brain, pancreas, bone, ovary, testes and tissues of the lower urinary tract. PGR is expressed via an oestrogen-regulated promoter. Some studies have investigated the role of PGR in particular forms of migraine, as females tend to be more prone to migraines.

Level of evidence star rating

★★
Evidence relating the T allele and altered receptor function

★★
Evidence relating the T allele with endometrial changes

What do your results mean?

The PGR T allele results in an amino acid change from valine (Val) to leucine (Leu) at position 660. The variant T allele (Leu amino acid) has been associated with altered expression and function of the receptor, which may lead to changes in ovulation and menstruation. The T allele has been associated with changes in the endometrium and an increased risk for endometriosis. In addition, the T allele is associated with an increased risk for migraine with vertigo.

Hormone Receptor And Thyroid > FOXE1

Gene	Gene variation	rs number	Result		Effect
FOXE1	57kb upstream G>A	rs965513	GG	- -	

Legend

- No effect
- Pay attention
- Pay close attention

- - Wild type
- - + Heterozygous
- + + Homozygous

Gene description

Forkhead Box E1 (FOXE1), also known as thyroid transcription factor 2 (TTF2), codes for a thyroid transcription factor that is involved in the regulation the transcription of thyroid hormones. FOXE1 is required for thyroid development and maintenance of both the pituitary and thyroid gland during adulthood. A genetic variation rs965513 located close to FOXE1 and has been associated with altered thyroid function and thyroid disorders.

Level of evidence star rating

★★★
Evidence relating the G allele with altered thyroid function and increased risk for hypothyroidism

What do your results mean?

The FOXE1 G allele has been associated with altered thyroid function and may increase risk for hypothyroidism. Thyroid disorders have been linked to a combination of genes and environmental factors such as nutrient status, radiation exposure and infections.