dnasmile

PLUS MERCURY TOXICITY

Oral and systemic health

Welcome

Control Positive

to your DNA Smile report

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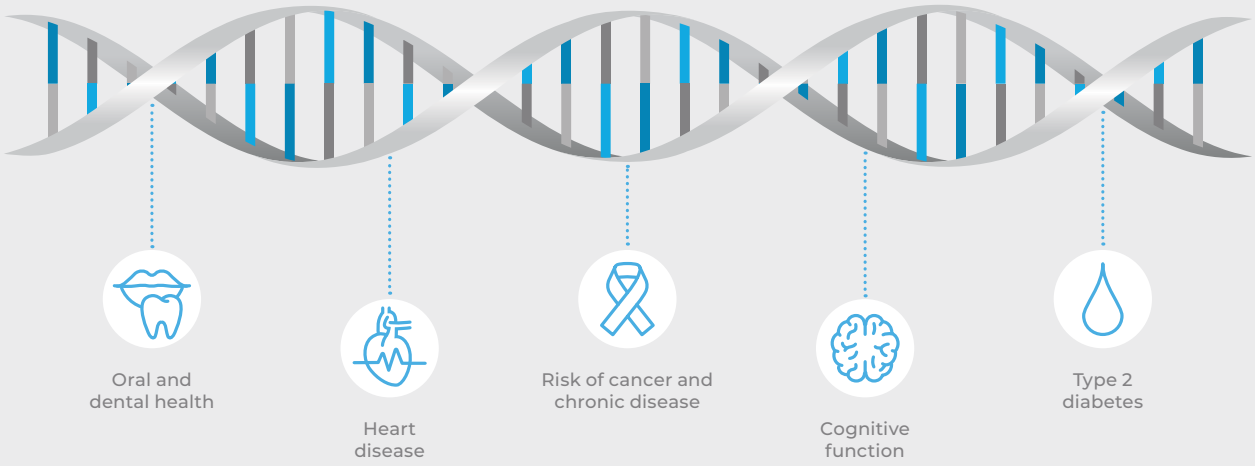
Referring practitioner: Nordic Laboratories

DNA Smile is a genetic test designed to give you insight into the state of your dental and oral health and risk for developing periodontal disease and tooth caries.



Genetics and personalised medicine

Genes are segments of DNA that contain the instructions your body needs to make each of the many thousands of proteins required for life. Each gene is comprised of thousands of combinations of "letters" (called bases) which make up your genetic code. The code gives the instructions to make the proteins required for proper development and function.

Genetic variations can affect the expression of a gene, thereby affecting metabolic processes that are important for maintaining cellular health and how we respond to environmental interventions such as diet, lifestyle, supplements, and medication.

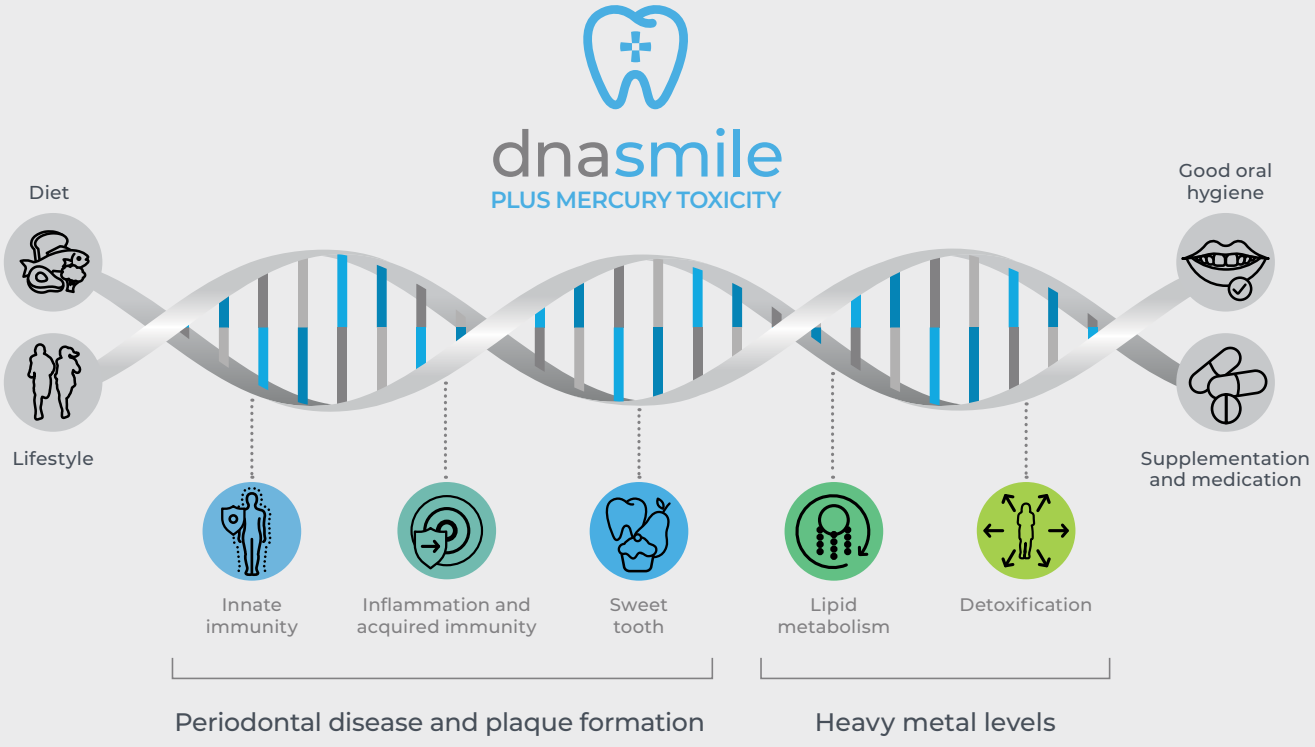
Knowledge of these genetic variations offers unparalleled insight into your biological systems, allowing your healthcare practitioner to recommend precise interventions aimed at helping you reach your goals and achieve optimal health.

NORMAL GENE
Genotype resulting in baseline potential for disease risk

VARIANT GENE
Genotype resulting in increased potential for disease risk and need for personalised intervention

Personalised medicine and dental health

Your oral health is strongly related to risk for development of chronic diseases, from cognitive decline to type 2 diabetes and heart disease. Early, targeted interventions using a holistic, systems-biology approach is essential to improve overall health outcomes. This report provides you with actionable information to improve oral health and prevent disease.



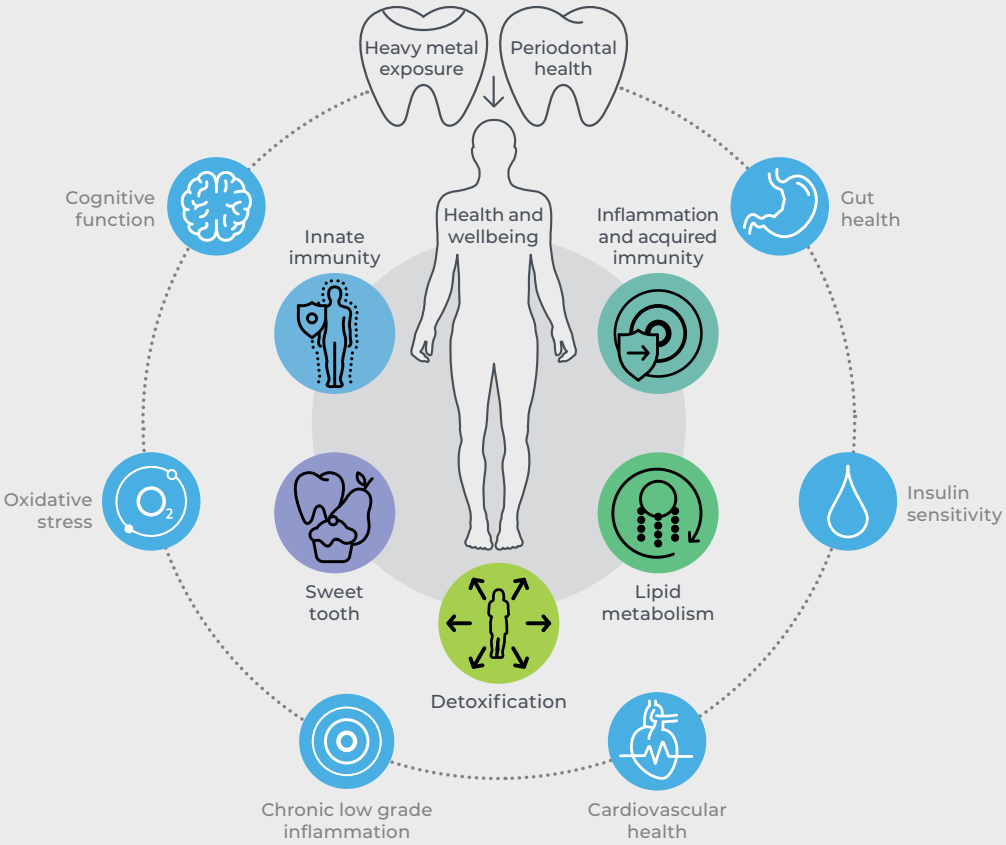
Understanding periodontal disease

Periodontal disease refers to both gingivitis (gum disease) and periodontitis. Periodontitis is a chronic inflammatory disease of the mouth that begins when bacteria, found in dental plaque, causes a major negative immune response, which leads to the damage of the connective tissue and the bones surrounding your teeth. If left untreated, the damage is irreversible and causes tooth loss.

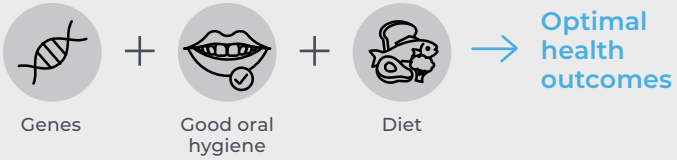
Your risk for developing periodontal disease is based on a number of factors, including oral hygiene practices, dietary intake (a high sugar intake), the presence of other inflammatory illnesses, exposure to certain pathogenic bacteria and an altered oral and gut microbiome, and, importantly, genetics.

Besides the importance of tending to your oral health to prevent tooth loss, is the relevance that your oral health has on the rest of your body. Periodontal disease has been strongly linked to an increased risk for a number of chronic inflammatory diseases, including cognitive decline and late-onset Alzheimer's disease, as well as heart disease, type 2 diabetes and certain cancers (oesophageal and oral cancer). Therefore, by understanding your risk for periodontal disease and ensuring good oral health with personalised interventions, you are also able to control and decrease your risk for other inflammatory diseases.

DNA SMILE CAN HELP IDENTIFY HEALTH RISKS:



To improve your health outcomes and reduce the risk of disease:
understand your risk and ensure good oral health with early targeted interventions



Result summary

BIOLOGICAL AREA	PRIORITY
Innate immunity	MODERATE
Inflammation and acquired immunity	HIGH
Sweet tooth	MODERATE
Lipid metabolism	LOW
Detoxification	MODERATE

Genotype results

○ No Impact ● Low Impact ●● Moderate Impact ●●● High Impact ✓ Beneficial Impact

BIOLOGICAL AREA	GENE NAME	GENE VARIATION	RESULT	GENE IMPACT
Innate immunity	DEFB	3'UTR c*5G>A	AA	●●●
		-44 C>G	GG	○
	TLR4	896 A>G	AA	○
		1196 C>T	CC	○
Inflammation and acquired immunity	IL-1A	-889 C>T	CC	○
		4845 G>T	GG	○
	IL1B	3954 C>T	CC	○
		-511 T>C	AA	○
	IL1RN	2018 T>C	TT	●●
	IL6	-174 C>G	GG	○
	IL17A	-197 G>A	GA	●●
	MMP3	Lys45Glu (A>G)	AG	●
	TNFA	G>A	AG	●●
Sweet tooth	SLC2A2	Thr110Ile (T>C)	CC	○
	TAS1R2	Ile191Val (G>A)	AA	●●●
Lipid metabolism	APOE	E2/E3/E4	E3/E2	✓
Detoxification	GSTM1	present/absent	Absent	●●●
	GSTP1	A>G	AA	○
	GSTT1	present/absent	Present	○

Gene results per biological area with personalised recommendations

Innate immunity

The innate immune system comprises physical defensive barriers such as the skin; defensive mechanisms such as saliva; and the general immune response, which includes immune cells and proteins. The innate immune system is activated by the presence of antigens and their chemical properties and depends on pattern recognition receptors (PRRs) to detect conserved structures of pathogenic microorganisms (like bacteria, virus, fungus and protozoa), which are called pathogen-associated molecular patterns (PAMPs).

Innate immunity results

Genotype result table:

GENE NAME	GENE VARIATION	RESULT	GENE IMPACT
DEFB	3'UTR c*5G>A	AA	●●●
	-44 C>G	GG	○
TLR4	896 A>G	AA	○
	1196 C>T	CC	○

Priority level: **Moderate**

Recommendation:

Your genotype results may lead you to have an altered innate immune response when exposed to endotoxins and harmful bacteria, thus moderately contributing toward an increased risk for developing periodontal disease as well as type 2 diabetes.

Stop smoking, if you smoke. Keep a healthy weight and follow a Mediterranean diet, which has been shown to be beneficial in improving inflammation. Avoid all refined carbohydrates, limit saturated fat intake, especially if you carry TLR4 variants, and ensure that you control blood glucose levels. Ensure good oral hygiene practices are followed.

Next steps:

Oral health assessment with your dental practitioner including lab tests for detection of periodontitis-aggravating bacteria.

Consider the following tests:

- ***DNA Diet*** for optimal weight management
- ***HbA1c*** for checking blood sugar levels
- ***Fasting Insulin*** to evaluate insulin levels.

Gene and genotype specific information

DEFB

The DEFB1 gene encodes the beta-defensin 1 protein. The defensin family is a group of microbicidal and cytotoxic peptides that are essential in the innate immune response. Beta-defensin 1 is an antimicrobial peptide implicated in the resistance of epithelial surfaces to microbial colonization. The SNP has been found to influence susceptibility to and severity of periodontal diseases.

Result: AA ●●●

The AA genotype is associated with an increased risk for both chronic and aggressive periodontitis. Do not smoke and keep blood glucose levels well-controlled. Ensure good dental hygiene and consult with your dentist regarding risk management. Follow an anti-inflammatory diet, avoid refined carbohydrates and sugars.

Result: GG ○

The GG genotype is associated with normal protein function.

TLR4

The TLR4 gene encodes the toll like receptor 4, which is found on the surface of immune competent cells and plays an important role in autoimmunity, occupying a significant position as a receptor recognizing pathogen-associated molecular patterns (PAMPs).

TLR4 has been shown to contribute to the host's susceptibility for periodontitis. TLR4 cytokine expression is significantly increased in both macrophages and gingival fibroblasts located in inflamed gingival tissues indicating its importance in the inflammatory process. The binding of bacteria lipopolysaccharides (LPS) to TLR4 on human gingival fibroblasts (HGFs) can activate various second messenger systems, such as the nuclear factor κB (NF-κB) pathway. These processes are closely associated with the destruction of periodontal tissue. The two TLR 4 variants, 896 A>G and 1196 C>T, reported here, are frequently inherited together.

Result: AA ○

The AA genotype is associated with normal receptor function.

Result: CC ○

The CC genotype is associated with normal receptor function.

Inflammation and acquired immunity

Acquired immunity, also referred to as adaptive immunity, develops over your lifetime as you are exposed to a vaccine, an infection or disease, or another person's antibodies. The acquired immune system is composed of specialised, systemic cells and processes that eliminates pathogens by preventing their growth.

Inflammation, and the inflammatory response, are important factors to consider with acquired immunity. Cytokines are molecules that are used for cell signalling. A major function of cytokines is for them to be able to communicate with neighbouring or distant cells in order to initiate an immune response. Cytokines are also used to trigger cell trafficking to a specific area of the body. Increased levels of pro-inflammatory cytokines have been associated with chronic, low-grade inflammation, which is an important contributing factor to many chronic diseases including periodontitis. Chronic, low-grade inflammation, is also associated with an exaggerated response to an infection, increasing risk for adverse outcomes.

Inflammation and acquired immunity results

Genotype result table:

GENE NAME	GENE VARIATION	RESULT	GENE IMPACT
IL-1A	889 C>T	CC	○
	4845 G>T	GG	○
IL1B	3954 C>T	CC	○
	-511 T>C	AA	○
IL1RN	2018 T>C	TT	●●
IL6	-174 C>G	GG	○
IL17A	-197 G>A	GA	●●
MMP3	Lys45Glu (A>G)	AG	●
TNFA	G>A	AG	●●

Inflammation and acquired immunity (continued)

Priority level: **High**

Recommendation:

Your genotype combination contributes toward an increased risk for chronic, low-grade inflammation and related inflammatory disorders, due to increased expression of pro-inflammatory cytokines and an altered immune response to endotoxin and bacterial exposure.

Manage weight and follow a Mediterranean diet, which has been shown to be beneficial in improving inflammation. Include anti-inflammatory foods such as red and blueberries, curcumin, ginger and naturally fermented products (yogurt and sauerkraut). Decrease intake of saturated fats, moderate intake of omega 6 fatty acids, and increase intake of omega 3 fatty acids. Focus on food sources of vitamins A, and C, and ensure adequate sun exposure to improve vitamin D levels. Collagen supplementation in certain cases should also be considered, together with supplementation of the key nutrients (vitamins, A, D and C), as well as a probiotic. Avoid all refined carbohydrates. Stop smoking, if you smoke. Ensure good dental hygiene practices are followed and discuss further risk management of periodontal disease with your dental practitioner.

Next steps:

Oral health assessment with your dental practitioner including measurement of MMP8 levels in saliva and detection of periodontitis-aggravating bacteria.

Consider the following tests:

- ***Hs-CRP*** for the evaluation of current inflammation and/or
- ***Bloodspot Fatty Acids*** for the evaluation of dietary balance of omega 3 and 6 fatty acids to evaluate if diet is impacting the inflammatory state.

Gene and genotype specific information

IL-1

Result: ●●

IL-1 has been increasingly implicated as an important leverage point in the inflammatory cascade, and IL-1 expression is therefore key in the pathogenesis of several chronic diseases. The biological activity of IL-1 involves the two agonists – IL-1alpha (IL-1A) and IL-1beta (IL-1B), specific IL-1 receptors, and an IL-1 receptor antagonist (IL-1RN), which is a negative regulator of the pro-inflammatory response.

IL-1 is a potent regulator of the extracellular matrix, where increased expression leads to activation of osteoclasts and thus cellular degradation.

Certain genetic variations in IL-1A, IL-B and IL-1 RN lead to a more active inflammatory response, and have been associated with increased risk for a number of chronic diseases including periodontitis.

Individuals with variations in IL-1A, IL-1B, or IL-1RN are associated with having increased IL-1 plasma concentrations and have been linked with a number of pro-inflammatory chronic diseases, including periodontitis, coronary artery disease, certain autoimmune diseases, and cancers. Increase intake of nutrients known to inhibit the secretion of pro-inflammatory markers.

IL6

Result: GG ○

Interleukin 6 is a pro-inflammatory cytokine that plays a crucial role in inflammation and regulates expression of CRP. This gene has been implicated in the development of periodontal disease and other chronic inflammatory diseases of lifestyle including low-grade chronic obesity and, insulin resistance, dyslipidaemia and increased risk for cardiovascular disease.

The GG genotype leads to normal expression of this gene and thus is not associated with an increased risk for chronic, low-grade inflammation.

Gene and genotype specific information (continued)

IL17A

Result: GA

IL-17A encodes the proinflammatory cytokine, Interleukin-17A, which is the most studied member of the IL-17 family, and is secreted by T helper-17 (Th-17) cells. It is a powerful activator of neutrophils and is contributing factor in the pathogenesis of various autoimmune and inflammatory diseases. IL-17 stimulates the production and expression of TNF-alpha and IL-1 beta by human macrophages and regulates antimicrobial activity of molecules such as calgranulins, β-defensins, and mucin. Increased levels IL-17 have been documented in the saliva of patients with periodontal disease.

The GA genotype leads to increased expression of IL-17A and higher serum levels of the proinflammatory cytokine have been found in IL-17A GA genotype carriers. The risk variant is associated with chronic periodontitis and is linked to worse clinical and inflammatory periodontal parameters. The GA genotype has also been shown to be a major contributor to the development of a number of inflammatory diseases including coronary artery disease and osteoarthritis. Obesity, a modern Western diet, and high levels of oral bacteria stimulate the production of IL-17A.

MMP3

Result: AG

Matrix metalloproteinases (MMPs) are involved in the breakdown of the extracellular matrix in normal physiological processes, such as embryonic development and tissue remodelling, as well as in disease processes, such as arthritis and metastasis. MMPs have been implicated as a significant mediator of periodontitis-associated tissue breakdown, due to their role in the pathological destruction of extracellular matrix and immune responses related to periodontal inflammation. MMP3 (stromelysin-1) can degrade collagen in the basal membrane and can induce the synthesis of other MMPs, such as MMP1, MMP8 and MMP9.

Individuals with the GA genotype are at an increased risk of developing periodontitis. The SNP is also related to a greater number of periodontal pockets as well as increased expression of MMP8 in the saliva. The MMP3 Lys45Glu variant alters the transcription levels of this matrix-degrading enzyme, affecting its ability to degrade connective tissue and thus may lead to the progression of periodontitis. Lifestyle factors, such as smoking, diet, and psychosocial conditions as well as comorbidities, such as diabetes and exposure to certain harmful bacteria in the mouth all contribute toward the development of periodontal disease.

TNFA

Result: AG

Tumour necrosis factor-α (TNFα), a proinflammatory cytokine secreted by both macrophages and adipocytes has been shown to alter whole body glucose homeostasis, and has been implicated in the development of several chronic diseases of lifestyle.

The GA genotype results in a two-fold increase in TNFA transcription, which leads to elevated levels of the circulating TNF protein. The A allele is associated with increased susceptibility for periodontal disease. This variant is also linked to an increased risk for obesity, dyslipidemia, and insulin resistance, especially in the presence of a modern Western Diet and when dietary saturated fat intake is high.

Sweet tooth

Higher sugar consumption has been strongly linked to the risk of obesity as well as developing tooth caries. Genetics contributes to the interindividual variability in sugar consumption, where sweet taste receptors and glucose sensors play an important role in influencing an individuals sweet craving behaviour and sugar intake and thus risk for tooth caries.

Sweet tooth results

Genotype result table:

GENE NAME	GENE VARIATION	RESULT	GENE IMPACT
SLC2A2	Thr110Ile (T>C)	CC	○
TAS1R2	Ile191Val (G>A)	AA	●●●

Priority level: **Moderate**

Recommendation:

Your genotype combination influences your ability to taste sweet foods, and may moderately contribute toward you having a “sweet tooth”, affecting your intake of high-sugar foods, and increasing risk for developing tooth caries, obesity, and type 2 diabetes. Avoid all sweet-tasting foods such as sweets and sweetened beverages, including those with artificial sweeteners. Maintain good oral hygiene practices.

Next steps:

Consider the following tests:

- ***HbA1c*** for checking blood sugar levels
- **Fasting Insulin** to evaluate your insulin levels

Gene and genotype specific information

SLC2A2

Result: CC

GLUT2, coded by the SLC2A2 gene, is a member of the facilitative glucose transport protein (GLUT) family and is expressed in the pancreas, liver, small intestine, kidney, and brain. GLUT2 facilitates the first step in glucose induced insulin secretion, with the entry of glucose into the pancreatic βcell. Because of its low affinity for glucose, it has been suggested as a glucose sensor, is considered to be important in the postprandial state, and is involved in food intake and regulation.

The CC genotype leads to a normal functioning receptor and has not been associated with adverse health outcomes.

TAS1R2

Result: AA

TAS1R2 encodes the taste receptor type 1 member 2, which is strongly involved in sensing sweet taste in foods, both from natural sugars as well as artificial sweeteners.

The AA genotype is associated with altered receptor function and individuals with this genotype have been reported to consume more high-sugar foods and sweet beverages, increasing susceptibility to developing tooth caries.

Lipid metabolism

APOE encodes Apolipoprotein E, a lipid-transporting protein functioning in both the periphery and the central nervous system, and is involved in multiple biological processes related to Alzheimer's disease (AD) development and progression. Two SNPs on APOE results in three possible isoforms. The isoform affects the structure and function of apoE including binding to lipids, receptors and Aβ.

Lipid metabolism results

Genotype result table:

GENE NAME	GENE VARIATION	RESULT	GENE IMPACT
APOE	E2/E3/E4	E3/E2	✓

Priority level: **Low**

Recommendation:

Based on your APOE genotype, there is no associated increased risk for periodontal disease and related systemic disorders. Manage weight and follow a healthy balanced diet as prescribed by your healthcare practitioner.

Gene and genotype specific information

APOE

Result: E3/E2

APOE encodes Apolipoprotein E, a lipid-transporting protein functioning in both the periphery and the central nervous system, and is involved in multiple biological processes of age-related diseases. Two SNPs on APOE results in three possible isoforms, ϵ2, ϵ3 and ϵ4. The isoform affects the structure and function of apoE including binding to lipids, receptors and Aβ.

The APOE E2 variant is associated with improved antioxidant capacity compared to other APOE genotypes. The APOE E2/E3 genotype may also confer protection against cognitive decline and late-onset Alzheimer's disease.

Detoxification

The detoxification process in the body is governed primarily by the GST family of enzymes. Glutathione S-transferases are responsible for catalysing reactions in which the products of Phase I metabolism are conjugated with glutathione, thus making them more water soluble and more easily excreted from the body through sweat and urine. Weaknesses in this area have been linked to increased risk for poor clearance of heavy metals and thus increase heavy metal load. Cruciferous and allium vegetables help increase the activity of your detoxification system, which aids the removal of harmful substances from your body.

Detoxification results

Genotype result table:

GENE NAME	GENE VARIATION	RESULT	GENE IMPACT
GSTM1	present/absent	Absent	●●●
GSTP1	A>G	AA	○
GSTT1	present/absent	Present	○

Priority level: **Moderate**

Recommendation:

Your genotype results indicate that you may have a moderately decreased detoxification ability and therefore an increased susceptibility to oxidative damage and related diseases, including cardiovascular disease and cognitive decline. Decrease exposure to environmental pro-carcinogens such as cigarette smoke, smoked and chargrilled foods, pesticides and other pollutants. If you have amalgam fillings, it is important to discuss risk-management strategies with your dental health practitioner, in order to reduce the possible heavy metal toxic load on your detoxification system. Support phase two detoxification by increasing intake of cruciferous (broccoli) and allium (onion) vegetables, daily, as well as selenium-rich foods (Brazil nuts) and vitamin C (citrus and kiwi fruit). Also ensure adequate intake of good quality protein.

Next steps:

Consider the following tests:

- ***Hepatic Detox Profile*** e (D-glucaric & Mercapturic Acids) for detoxification status, or
- ***Organix Comprehensive*** which includes detoxification indicators and the 8-Hydroxy-2-deoxygaunosine marker for the evaluation of oxidative stress, and
- *Tests for heavy metal toxicity*

Gene and genotype specific information

GSTM1

Result: **Absent**

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

A deletion results in an absence of the enzyme, leading to reduced capacity for hepatic detoxification and increased risk of various cancers, chemical sensitivity, coronary artery disease in smokers, atopic asthma, and deficits in lung function, as well as increased risk of heavy metal burden in exposed individuals.
Follow a diet rich in antioxidants and minimize exposure to toxins including heavy metals such as those from amalgam fillings.

GSTP1

Result: **AA**

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

The AA genotype is associated with normal enzyme function.

GSTT1

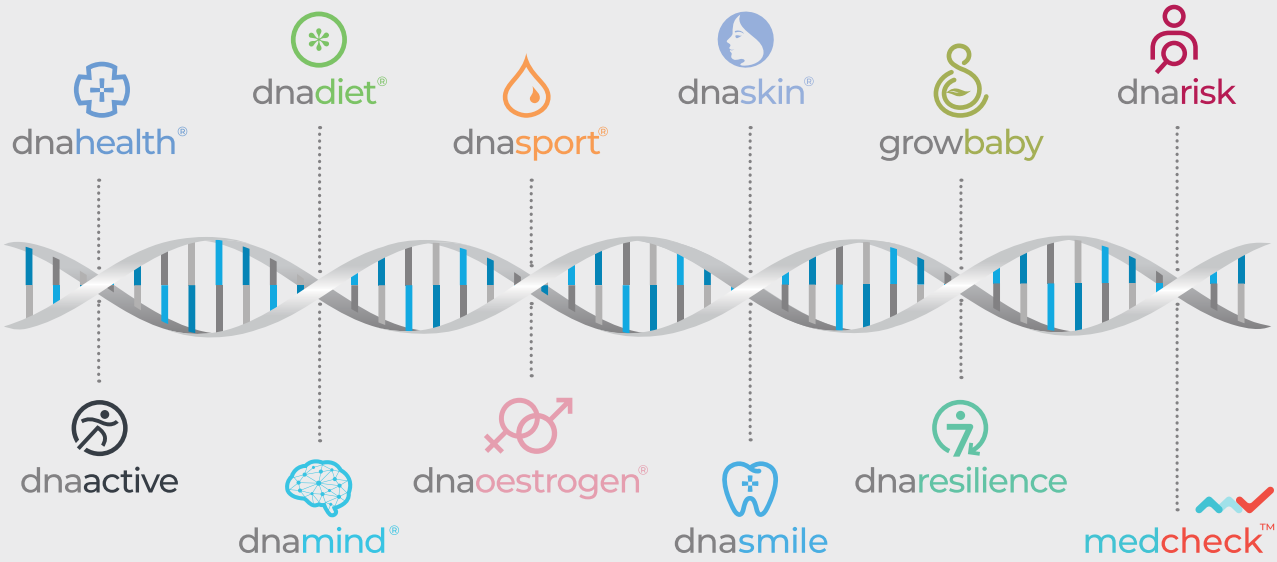
Result: **Present**

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

The insertion genotype leads to a present gene, which is associated with normal enzyme function.

A lifetime of optimal health awaits you

Your genes do not change, which means our laboratories will only ever need one sample* from you. Throughout your life, as your health goals and priorities change, we can continue to provide valuable health insights from this single sample* to support your unique health journey.



Requires finger prick blood spot sample collection

Our Commitment

DNAlysis Biotechnology is continuously developing new tests with the highest standards of scientific rigour. Our commitment to ensuring the ethical and appropriate use of genetic tests in practice means that gene variants are only included in panels once there is sound motivation for their clinical utility and their impact on health outcomes.

ADVANCED technology | ACTIONABLE interventions | APPROPRIATE use in practice

From the laboratories of:

DNALYSIS Biotechnology

Distributed by:

dnalife® Nordic Laboratories

info@dnalife.healthcare | www.dnalife.healthcare

For more information:
011 268 0268 | admin@dnalysis.co.za | www.dnalysis.co.za

Approved by:
Thenusha Naidoo - Medical Scientist
Larisa Naguriah - Medical Technologist
Danny Meyersfeld (PhD) - Laboratory Director

Denmark Office: Nygade 6, 3.sal · 1164 Copenhagen K · Denmark | **T:** +45 33 75 10 00
South Africa Office: North Block · Thrupps Centre · 204 Oxford Rd · Illovo 2196 · South Africa | **T:** +27 (0) 11 268 0268
UK Office: 11 Old Factory Buildings · Battenhurst Road · Stonegate · E. Sussex · TN5 7DU · UK | **T:** +44 (0) 1580 201 687

Risks and Limitations:
DNAlysis Biotechnology has a laboratory with standard and effective procedures in place for handling samples and effective protocols in place to protect against technical and operational problems. However as with all laboratories, laboratory error can occur; examples include, but are not limited to, sample or DNA mislabelling or contamination, failure to obtain an interpretable report, or other operational laboratory errors. Occasionally due to circumstances beyond DNAlysis Biotechnology's control it may not be possible to obtain SNP specific results.