DNA blue

Well Man Genetic Report

Table of Contents

Gene Contents

Welcome to your unique DNA-based Male Health Report. The contents of this report will highlight your ***potential* genetic strengths and weaknesses** in hormone production and detoxification, as well as other genetic factors that affect male health and well-being at all ages such as heart, vascular, prostate and bone health, and fertility. This information is useful on its own but is highly recommended together with hormone and other functional tests in order to provide you with the most complete picture of current and future health.

Please be assured that your genes are ***NOT*** your destiny. Having one or multiple genetic variants may increase risk, however, many health concerns can be reversed and/or avoided by assessing risk factors and implementing recommended diet and lifestyle measures.

Our advice and recommendations are based on **your specific genotype** in each of these areas.

We invite you to come along on this journey to reaching optimal hormone health - one ***YOU*** can be in control of!

Let's get started…

Understanding your report

What is DNA?

DNA is your body's unique instruction manual, controlling every single function from when you were made up of only a few cells, until now. DNA looks like a twisted ladder, made up of two halves.

Each "rung" of the ladder contains two "letters" of DNA code called ***nucleotides*** which bond together in pairs: **A (adenine)** and **T (thymine)** bond together**,** as do **C (cytosine)** and **G (guanine).**

Genes are portions of the ladder containing combinations of the nucleotide code which are "read" as instructions to perform a specific function.

SNPs

Over time, due to environmental and lifestyle factors, minor changes called **single nucleotide polymorphisms (SNPs)** occur within the DNA code and are passed down from parent to child, from generation to generation. Remember the nucleotides? Well, a C might be replaced by a T, changing the instruction manual slightly.

Some SNPs are positive, making us stronger and more resilient (like being able to digest milk after infancy), some are negative (like being likely to store more fat as a result of past famine or food shortage) and some make no difference at all. SNPs can be passed down from just one parent, or from both, enhancing the effect. SNPs are generally what we are looking for when we test your DNA.

Results

Your results are shown by a combination of the letters **ATCG** along with a traffic light system to indicate if your result is beneficial, neutral or potentially negative.

Identical letters (e.g. GG or AA) mean you are either what is called the **wild type** with no genetic variants (SNPs) OR you have **both** genetic variants (from both parents). A combination of letters (e.g. AG) means you have one inherited genetic variant.

A green result indicates either no variants or a positive variant impact

An amber result usually indicates one genetic variant present and / or a mildly negative impact

A red result indicates a negative impact either due to both variants being present or a wild type result that is not as beneficial as the variant

Example of your genetic results

GENE	RESULT	IMPACT & ADVICE
GENE CODE - Gene Function Explanation of the role the gene plays and what effect genetic variants might have, symptoms, other contributing factors.	**GG**	An explanation of your result, how you might be affected along with specific diet and lifestyle advice
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Testosterone

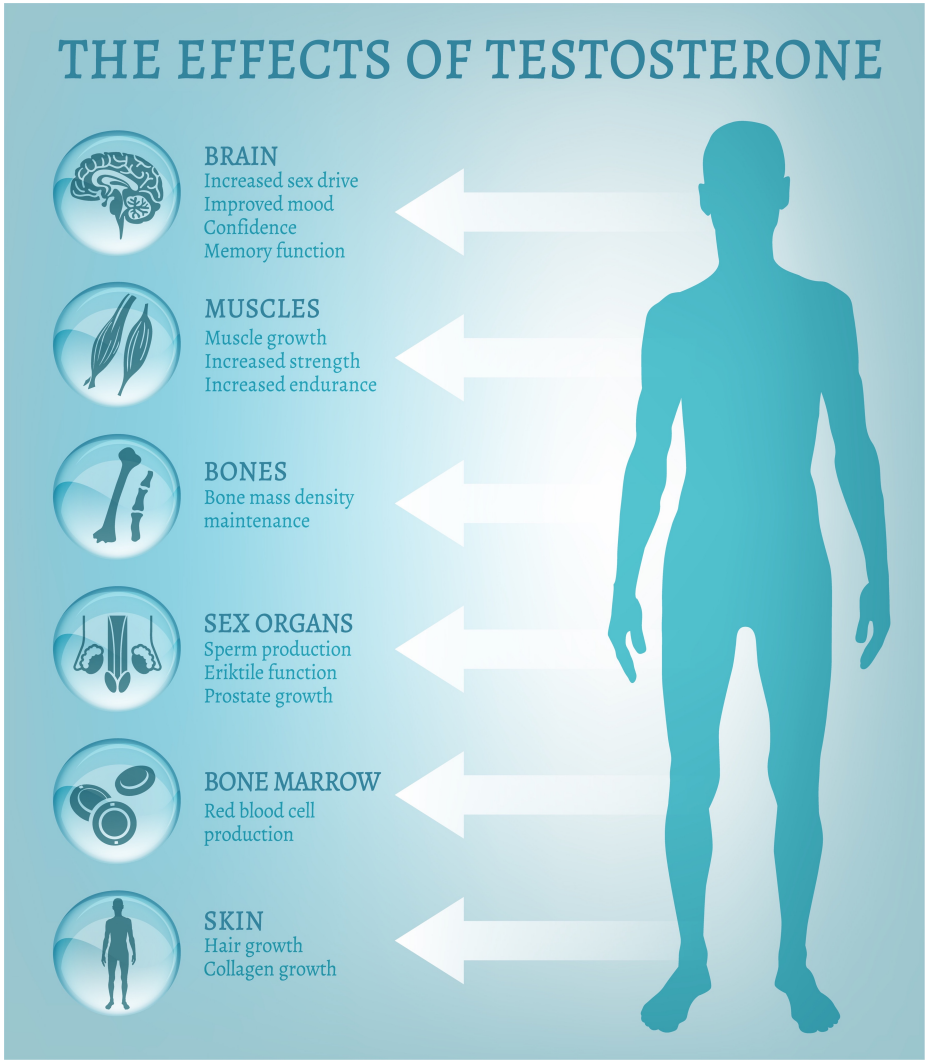
Testosterone is the main steroid hormone (androgen) in men responsible for sex drive, enlargement of the penis, sperm production & development, increased muscle mass, fat distribution, red blood cell production and lowering of the voice. Most of the testosterone in men is produced in the testes, while a smaller amount is made by the adrenal glands.

Luteinising hormone (LH) and **follicle-stimulating hormone (FSH)** are two hormones produced in the brain which stimulate the production of testosterone and sperm respectively.

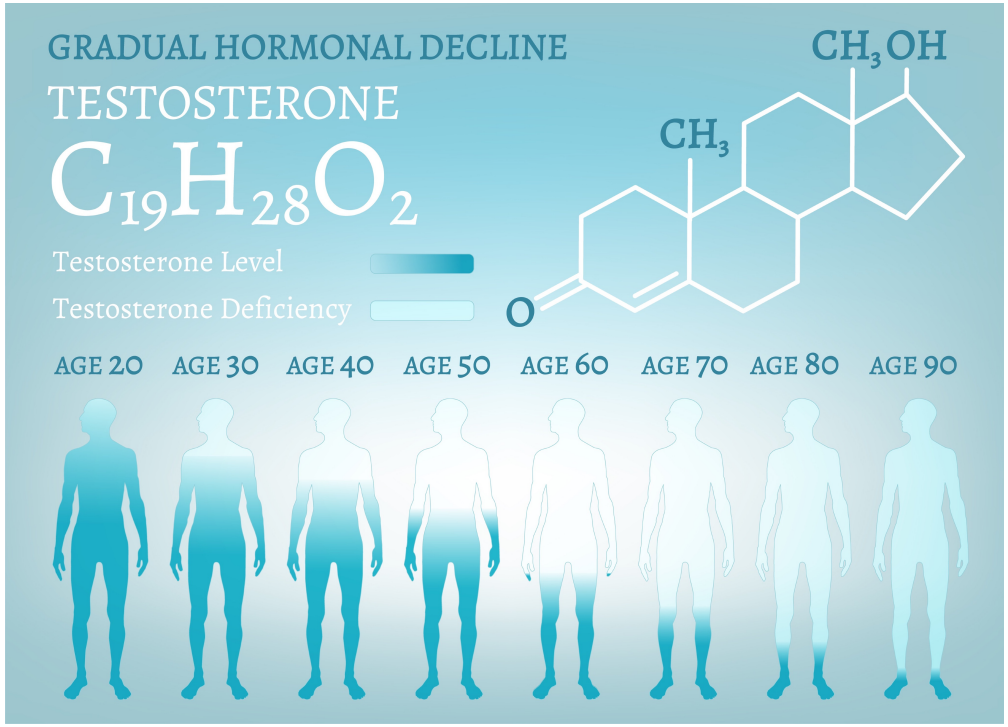
Once produced, testosterone is bound and transported in the blood by the protein, **sex hormone binding globulin (SHBG)** and, to a lesser extent, by albumin. To become active, testosterone must be released from SHBG and bind to **androgen receptors (ARs)** in target tissues.

Testosterone is also converted into two other important hormones: **5a-dihydrotestosterone (DHT)** and **oestrogen.**

DHT is about 3-5 times more potent than testosterone because it binds more strongly to the ARs. While DHT is important for developing and driving normal male characteristics, its strong androgenic action is also responsible for increased hair growth and eventually loss, acne and enlargement of the prostate gland in later life.



Testosterone Levels



Symptoms of low testosterone:

Low sex drive, erectile problems, low semen volume, fatigue, insomnia, loss of muscle mass, increased body fat, decreased bone mass and mood changes

Symptoms of high testosterone:

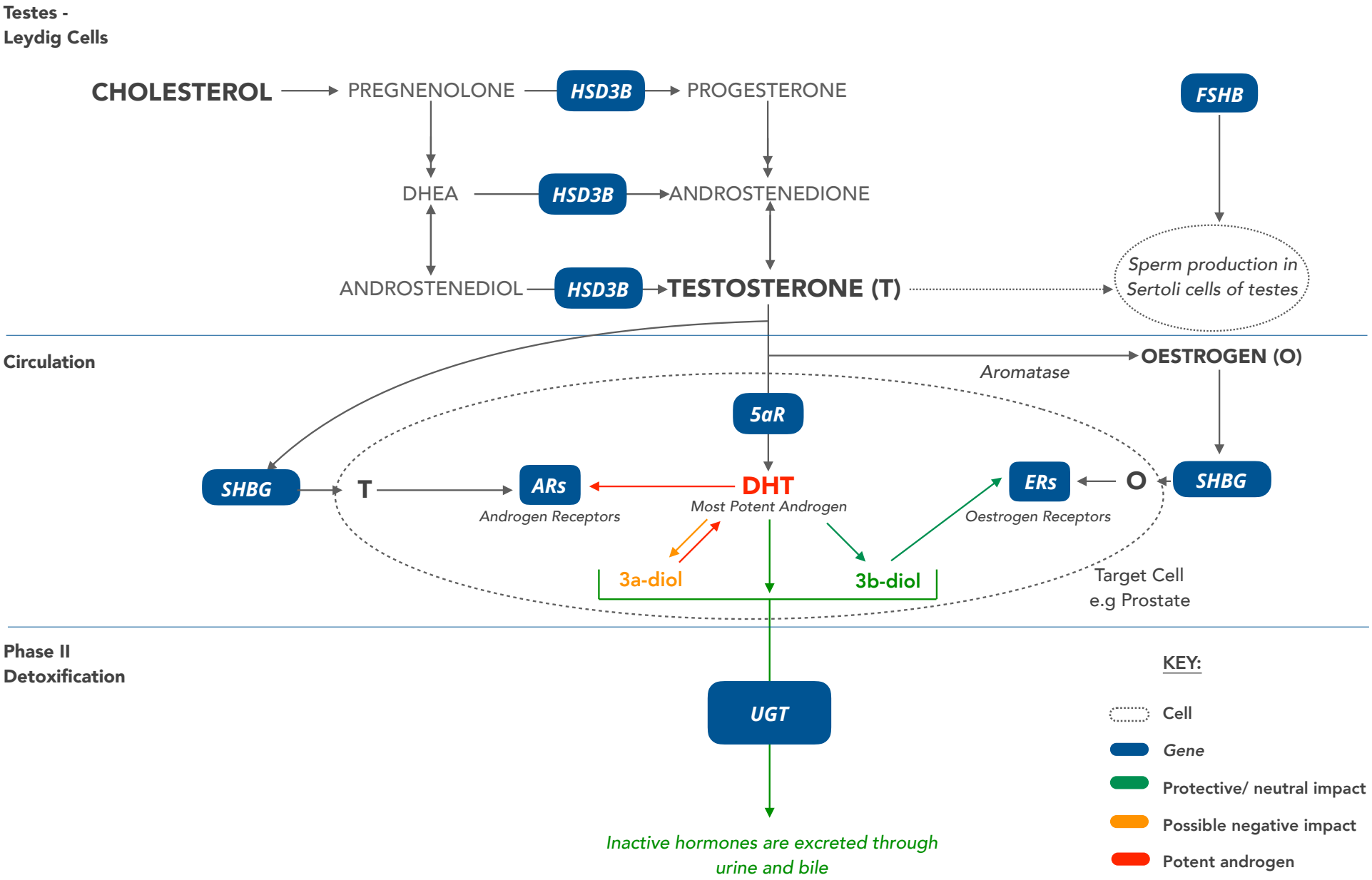
Acne, enlarged prostate, balding, fluid retention, reduced testicle size, decreased sperm count and increased red blood cells

Maintaining a healthy testosterone level is extremely important for overall health and well-being in men. Both high and low testosterone can have a negative impact. Healthy males make about 3-10mg of testosterone per day.

Common factors affecting testosterone levels:

- **Age:** testosterone levels gradually decrease with age. This is sometimes referred to as "andropause"
- **Exercise:** resistance training naturally increases testosterone levels. Lack of exercise can result in low testosterone levels
- **Nutrients:** low levels of vitamin D and zinc can contribute to low testosterone. Magnesium increases free and total testosterone in the body [1]
- **Weight:** lean body weight contributes to healthy testosterone levels. Increased body fat can lead to higher oestrogen levels and lower testosterone
- **Sleep:** the majority of daily testosterone release occurs during sleep. Poor sleep can lead to low testosterone levels [2]
- **Genetics:** your genes affect many factors that impact your testosterone levels

Male Steroid Hormone Metabolism

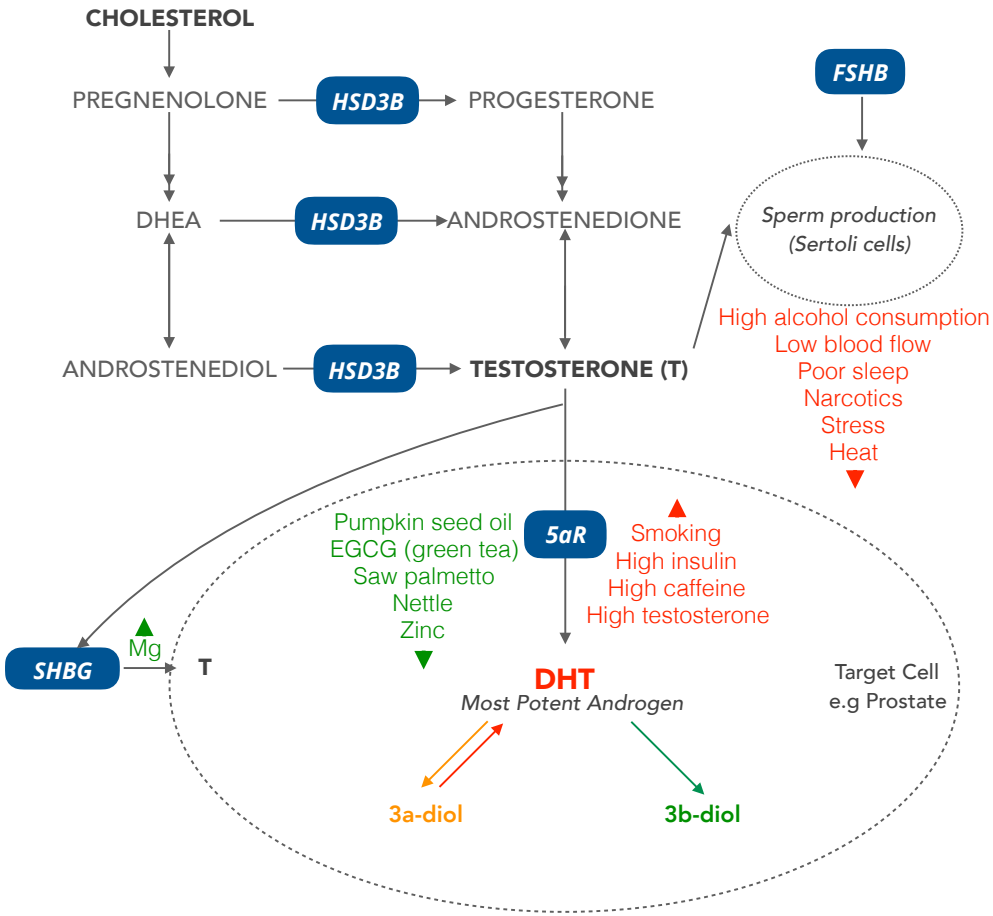


Androgen Production

Androgens (including T & DHT) are produced in the body via a series of steps from cholesterol. In males this occurs predominantly in the Leydig cells of the testes, and to a lesser extent in the adrenal glands. Androgens are hormones that regulate the development and maintenance of male characteristics in the human body. DHEA, androstenedione, testosterone and DHT are all examples of androgens. **Testosterone is the most abundant androgen** in males, while **DHT is the most potent**. The ***HSD*** family of enzymes play a large role in the production and maintenance of androgen levels in the body.

About **50-60% of T is bound and carried** in the blood to target cells such as the prostate, muscles, skin and hair follicles by **SHBG.** About **1-2%** of T **circulates unbound (free T**). About **10% of free T (fT)** is converted to **DHT** by the enzyme ***5a-reductase (5aR)***. DHT can then be converted into the metabolites ***3a-diol*** and/or ***3b-diol*** which are not androgens. **3a-diol** can be converted back into potent DHT which is why it is not considered positive, whereas ***3b-diol*** is reported to have a protective effect against prostate enlargement and tumours [1] [2].

Separately, ***FSH*** works together with T to stimulate the production and development of sperm in the Sertoli cells of the testes.



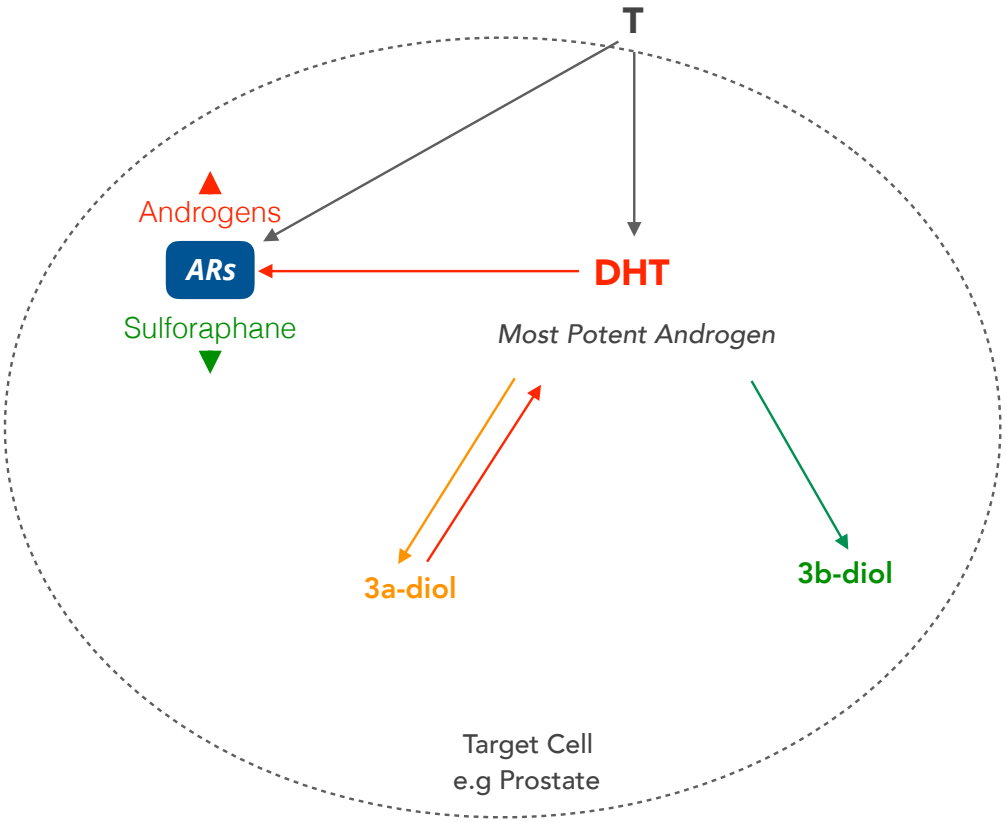
The ***HSD*** and ***5aR*** genes influence androgen levels in the body while ***SHBG*** influences amount of free T (fT). Variants in ***FSHB*** can lead to poor sperm production and infertility. Check your genetic results and advice on *pages **10 -12** below.*

GENE	RESULT	IMPACT & ADVICE
FSHB - Sperm Production & Fertility The FSHB gene controls the production of follicle stimulating hormone subunit beta (FSHB) in the brain (pituitary gland) which, in combination with T, drives sperm production and development in the Sertoli cells of the testicles. Healthy males produce approximately 120 million sperm daily. Anything below 15 million sperm/ml of semen is considered low. Population studies have shown that 30-40% of infertility in couples is due to the male. The T result of the reported variant (-211GT) has been linked to low FSH levels which in turn is associated with reduced sperm production and poor fertility. Other factors that negatively affect sperm production include reduced blood and oxygen flow to the testes (e.g. tight underwear, saunas, cycling), alcohol and drug abuse, exposure to toxic chemicals, heavy metals, radiation or x-rays, prolonged physical and emotional stress, poor sleep, obesity and low levels of vitamins A, B-complex, D, and zinc.	**GG**	The GG genotype is associated with normal (not reduced) serum FSH levels. This is positive because FSH is essential for normal sperm production and development. To ensure healthy sperm production avoid excessive alcohol consumption, wear underwear that allows blood and oxygen flow to the testes, avoid hot tubs and saunas, get ample sleep, address your stress levels and diet (see page 30 for more healthy diet & lifestyle advice).
HSD3ß1 - Androgen Levels (Target Cells) HSD3ß1 belongs to the HSD family of enzymes which are involved in the production of various steroid hormones, particularly androgens. HSD3ß1 is expressed mostly in the liver, skin, kidneys and prostate gland in men which is why it is thought to be involved in regulating androgen levels in these and other target cells. The C result in the reported variant (N367T) is associated with higher androgen levels, particularly DHT. High DHT is thought to be involved in hair growth and eventually loss, enlargement of the prostate gland, bladder and urinary problems and certain cancers if levels remain consistently high. The AC and CC genotypes are more common in Caucasian, intermediate in African, and less common in Asian men.	**AA**	The AA genotype is most common in Asian populations and is linked to normal (not increased) androgen levels in target cells. This is positive since high androgen levels can increase risk of various androgen-linked conditions (see left for list).

GENE	RESULT	IMPACT & ADVICE
HSD3ß2 - Androgen Levels (Circulating) HSD3ß2 belongs to the HSD family of enzymes which are involved in the production of various steroid hormones, particularly androgens. HSD3ß2 is expressed almost exclusively in the adrenal glands and testes and is thought to be involved in regulating systemic (circulating) androgen levels. High DHT is thought to be involved in hair growth and eventually loss, enlargement of the prostate gland, bladder and urinary problems and certain cancers if levels remain consistently high. The T result in the reported variant (B2-c7519g) is more common in African, intermediate in Asian and rare in Caucasian populations. The T result, if inherited along with a C result for the N36T variant above, strongly increases likelihood of high androgen levels.	**CC**	The CC genotype is linked to normal (not increased) systemic levels of DHT. This is positive since high DHT levels can increase risk of various conditions such as hair loss and enlarged prostate (see left for more).
SHBG - Free Testosterone Levels The SHBG gene regulates the production of the protein, sex hormone binding globulin (SHBG), by the liver. The role of SHBG in the body is to bind the hormones T, DHT and oestrogen to carry them in the blood to target tissue. While bound to SHBG, hormones are inactive. As a result, high levels of SHBG can lead to low levels of free hormones, whereas, low levels of SHBG can result in high levels of free hormones. SHBG naturally increases with age and also with obesity, increased oestrogen levels, hyperthyroidism and liver disease. Magnesium is helpful for releasing T from SHBG when SHBG levels are high and T is low. Hypothyroidism causes SHBG levels to decrease, increasing free hormone levels. The A result in the reported variant (−68 GA) is associated with high SHBG levels.	**GG**	The GG genotype is associated with normal (not increased) SHBG levels and is therefore not a risk factor for low free testosterone levels. See page 7 above for a list of symptoms of low and high testosterone levels, and of other factors that can contribute to low (and high) levels. Follow the healthy nutrition and lifestyle advice on page 30.

GENE	RESULT	IMPACT & ADVICE
5aR1 - Testosterone to DHT (Serum) 5aR1 (also known as SRD5A1) is an enzyme responsible for converting T into DHT mostly in tissue outside of the prostate such as the adrenal glands, brain, skin, digestive tract, liver, kidney and thyroid. For this reason 5aR1 is thought to be involved in circulating (serum) DHT levels. High DHT drives hair growth and eventually loss, enlargement of the prostate gland, bladder and urinary problems and even certain cancers. As a result, the 5aR enzymes are the target of anti-androgen drug, Dutasteride, prescribed to reduce hair loss and enlarged prostate gland. 5aR enzyme activity is reportedly naturally lower in Asian populations than African and Caucasians. The C result in the reported 5aR1 variant (rs1691053) is associated with increased serum DHT levels.	**TT**	The TT genotype is associated with normal (not increased) 5aR1 activity and normal (not increased) serum DHT levels. This is positive because high DHT levels have been associated with androgen-linked conditions such as hair loss and enlarged prostate gland. Smoking, high caffeine intake and high insulin levels increase 5aR activity regardless of genetics. Specific substances that reduce 5aR activity include pumpkin seed oil, green tea, saw palmetto, nettle and zinc.
5aR2 - Testosterone to DHT (Target cells, particularly prostate) 5aR2 (also known as SRD5A2) is an enzyme responsible for converting T to DHT in target cells, particularly the prostate and testes. High DHT levels are linked to conditions like excessive hair growth and eventually loss, prostate enlargement, bladder and urinary problems, and even certain cancers. Finasteride and Dutasteride, two anti-androgen medications used to reduce hair loss and/or enlarged prostate gland work by reducing 5aR2 enzyme activity. A rare mutation (not reported here) inactivates the 5aR2 enzyme and results in poor development of male genitalia. Here we report two variants (V89L and A49T) on the 5aR2 gene known to affect 5AR2 enzyme activity.	**CC**	The CC genotype of this V89L variant is associated with approximately 40% lower 5aR2 activity and therefore reduced conversion of testosterone to DHT in the prostate and testicles. This is positive since high DHT levels in the prostate can lead to androgen-linked conditions such as prostate enlargement. This variant is thought to be dominant over the A48T variant below, helping to reduce overall levels of DHT. Smoking, high caffeine intake and high insulin levels increase 5aR activity regardless and should be avoided. Specific substances that help to naturally reduce 5aR activity include pumpkin seed oil, green tea, saw palmetto, nettle and zinc.
	CC	The CC genotype of this A49T variant is associated with normal (not increased) 5aR2 activity and normal (not increased) conversion of testosterone to DHT. This is positive since high DHT has been shown to increase risk of androgen-dependent conditions such as male pattern balding and benign prostatic hyperplasia (BPH). Smoking, high caffeine intake and high insulin levels increase 5aR activity regardless of genetics. Specific substances that help to naturally reduce 5aR activity include pumpkin seed oil, green tea, saw palmetto, nettle and zinc.

Androgen Receptors



Genetic variants on the ***AR*** gene affect the function of the AR in cells. Check your result on *page **14** below.*

The androgen receptor (AR) is a type of receptor found in various cells and tissues such as bone, prostate, hair follicles and adipose (fat) tissue, and plays a role in the development and maintenance of the **reproductive, musculoskeletal, cardiovascular, immune and nervous systems**. ARs are activated by **binding to androgens**, including T and DHT. The main function of the AR is **regulating the expression** (switching "on" or "off") of genes which promote the development of male sexual characteristics, and **controlling the growth and death** of cells.

DHT binds more strongly to the AR, making it's potency around **3-5 times stronger than testosterone.** Although DHT is necessary for normal growth and development, consistently high levels can lead to **high AR activation in cells**, which in turn can lead to excessive hair growth and eventually loss, enlargement of the prostate gland and some types of cancer. For this reason the AR is an important target for prostate cancer drugs.

The DHT metabolites, ***3a-diol*** and ***3b-diol*, do not bind to ARs** and are thus not considered to be androgenic. ***3b-diol*** has actually been found to be protective against high androgen conditions due to the fact that it binds to **oestrogen receptor beta (ESR2)** which has anti-androgenic effects (see more on oestrogen receptors on page 15).

GENE	RESULT	IMPACT & ADVICE
AR - Androgen Receptor The AR gene regulates the activity of the androgen receptor (AR) in cells. ARs enhance the effect of the attached androgen (e.g. T and DHT) and are critical for the development and maintenance of typically male characteristics depending on where in the body the receptor is located. Androgens play a key role in male skeletal integrity, muscle and hair growth, and prostate health. The AR gene is located on the X (female) chromosome which indicates the importance of the maternal line in the inheritance of conditions such as male-pattern baldness. The Stul variant, reported here, has been strongly associated with male-pattern balding and also with elevated PSA levels.	**GG**	The GG genotype is common in men with male-pattern hair loss (particularly in Caucasian populations), and is also associated with elevated PSA levels which is linked to prostate enlargement. Since ARs are activated by the attached androgen, a priority for this genotype is to keep DHT levels in check by reducing 5aR activity (see page 12) and encouraging elimination (see pages 17 & 18). Sulforaphane, a compound found in cruciferous vegetables, helps to encourage hormone elimination and has been found to specifically reduce AR activity.

Oestrogen & Oestrogen Receptors

Although typically associated with females, a small amount of oestrogen is necessary for bone and cardiovascular health, as well as balanced mood and brain function in men. In both sexes T is produced first and then converted to oestrogen by an enzyme called ***aromatase***. See diagram (right) for factors that **increase and decrease aromatase activity.**

High oestrogen is more of a problem for men than low, especially as they age and testosterone levels naturally decrease. This is because **oestrogen is known to stimulate cell growth** and is thought to be involved in driving prostate enlargement and certain cancers, rather than just DHT alone [1].

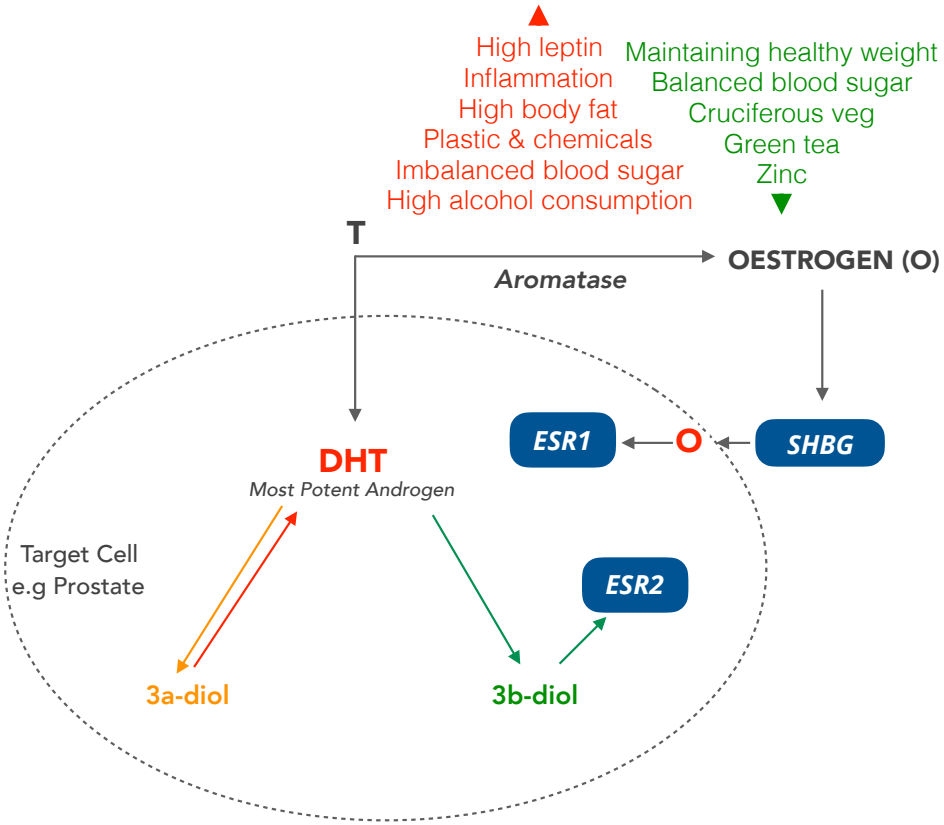
Like androgens, oestrogen exerts its influence in the body by attaching to **oestrogen receptors (ERs)** in target cells. There are two types of ERs:

- **ESR1** - increased oestrogen activity
- **ESR2** - decreased oestrogen activity

Since **ESR1** is known to enhance the effect of the attached oestrogen, it is thought to play a direct role in driving cell growth.

ESR2, on the other hand, is thought to be protective. For this reason, the DHT metabolite, ***3b-diol,*** is thought to be protective against prostate growth and certain types of cancer.

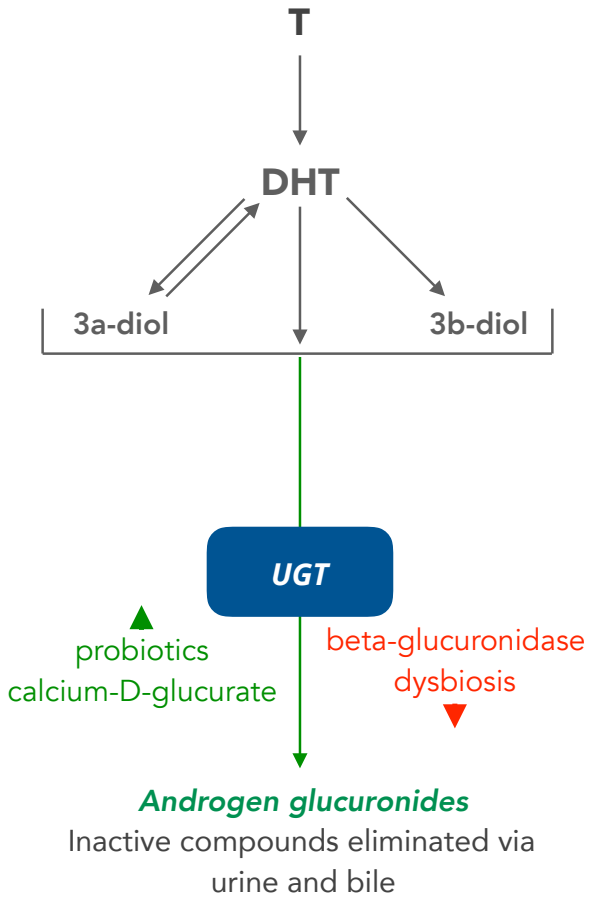
Symptoms of high oestrogen in men include: increased body fat (including "man boobs"), low sex drive, mood and energy



Increased ***ESR1*** activity enhances the effect of oestrogen attached to the receptor. Check your result on page ***16***

GENE	RESULT	IMPACT & ADVICE
ESR1 - Oestrogen Receptor 1 (alpha) The ESR1 gene regulates the activity of the oestrogen receptor alpha (ERa) which is involved in binding, activating and enhancing the attached oestrogen. In males, ERs are found in reproductive tissue such as the testicles and prostate, as well as nonreproductive tissue such as brain, liver, muscle and kidney cells. ESR1 is necessary for oestrogen to be effective in the body however, if oestrogen levels and activation are consistently elevated this can eventually play a role in prostate enlargement and cancer. Here we report two variants (Pvull and Xball) known to influence ESR1 activity in Caucasians but not in Asian populations.	**CT**	The CT genotype for the Pvull variant is associated with moderately increased ESR1 function and therefore increased enhancement of attached oestrogen. This is considered negative, especially if oestrogen levels are high, since oestrogen is known to play a role in driving prostate enlargement and certain oestrogen-linked conditions. Maintaining a healthy weight, balancing blood sugar and eating a varied diet that includes green vegetables will help to naturally keep oestrogen production (aromatase) in check. See the diagram on page 15 for factors that increase aromatase and page 30 for more healthy diet and lifestyle advice.
	GA	The GA genotype in the Xball variant is associated with increased ESR1 function and therefore increased enhancement of attached oestrogen. This is considered negative, especially if oestrogen levels are high, since oestrogen is known to play a role in driving prostate enlargement and certain oestrogen-linked conditions. Maintaining a healthy weight, balancing blood sugar and eating a varied diet that includes green vegetables will help to naturally keep oestrogen production (aromatase) in check. See the diagram on page 15 for factors that increase aromatase, and page 30 for more healthy diet and lifestyle advice.

Androgen Elimination



Variants in ***UGT*** can lead to poor elimination of T, DHT and their metabolites. See *page* ***18*** *for your results.*

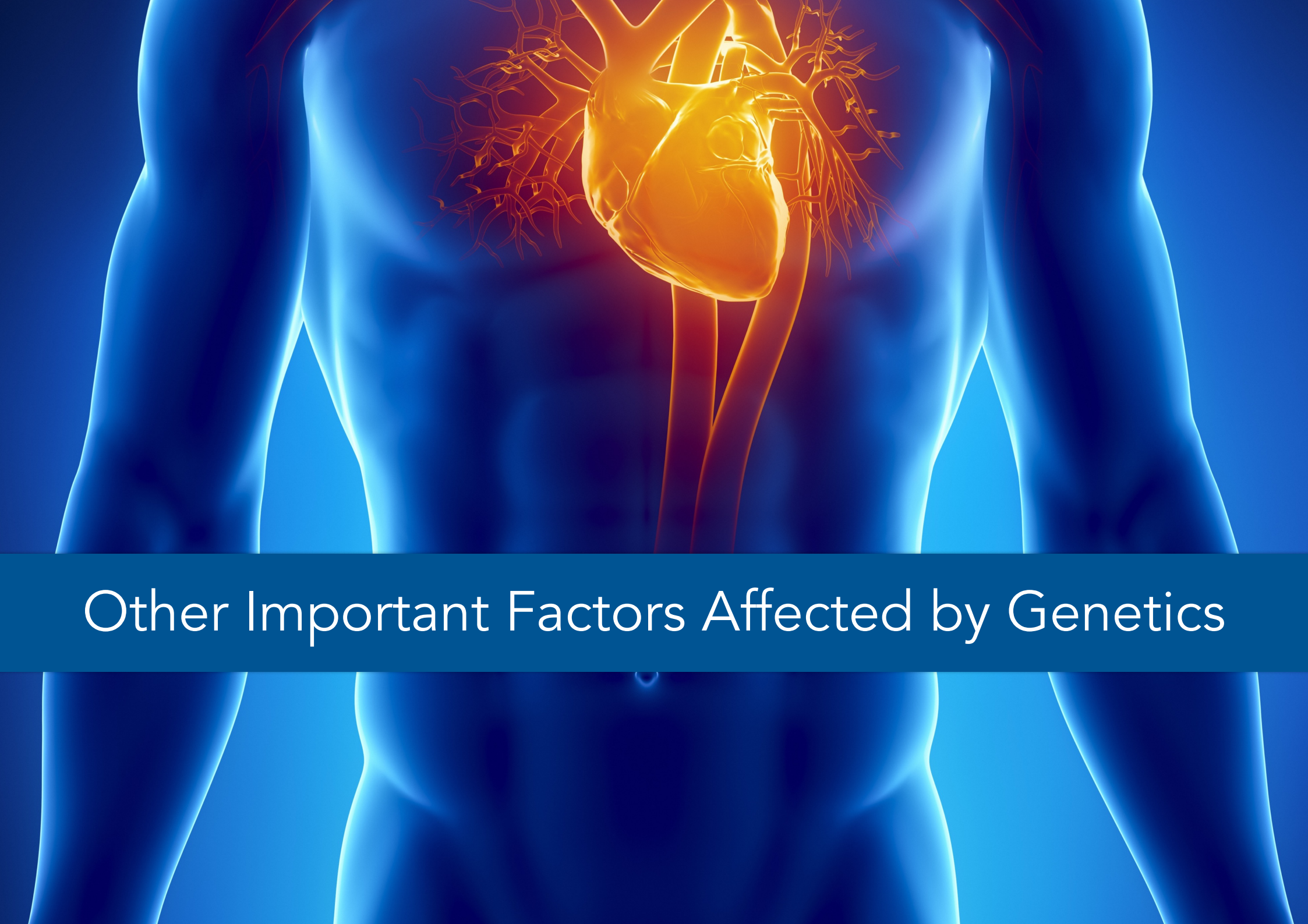
In order for androgens to be eliminated from the body, they must first be **inactivated**. The major sites for inactivation of hormones are the **liver and kidneys**. Some inactivation also occurs directly within **target cells**. Inactive hormones are then eliminated from the body via the **urine and bile (stool)**.

Inactivation of hormones occurs via a process called ***conjugation***. The major conjugation pathway for T, DHT and their metabolites is a phase II detoxification reaction called ***Glucuronidation*** which occurs via the ***UGT*** family of enzymes [1]. The resulting **androgen glucuronides do not bind to ARs** and are, therefore, **biologically inactive. Oestrogens are also eliminated** via this pathway to an extent.

An enzyme called **beta-*glucuronidase*** is able to unbind conjugated hormones, releasing them back into circulation. Humans naturally produce a **small amount of beta-glucuronidase**, however, the **majority of this enzyme** is released in the digestive tract by the **E.coli bacteria**. For this reason, **imbalanced gut microbes (dysbiosis)** can lead to **poor detoxification of hormones**. A substance called **calcuim-D-glucarate**, found mainly in foods such as cruciferous vegetables, oranges and apples, and also produced by humans in small amounts, has been shown to **inhibit beta-glucuronidase** [2]**.**

Androgens can also be inactivated via ***sulphotransferase (SULT) enzymes***. Since this is not the major pathway of elimination for T, DHT and metabolites, we do not focus on these genes in this report.

GENE	RESULT	IMPACT & ADVICE
UGT2B15 - Androgen Glucuronidation The UGT2B15 gene encodes an enzyme expressed predominantly in the liver and gall bladder, responsible for the inactivation and elimination of various substances including androgens and oestrogens (steriod hormones) and some pharmaceutical drugs (e.g. anti-anxiety medication and Paracetamol). Inactivation of substances via this pathway is called glucuronidaion. UGT2B15 is the main pathway of elimination for the 3a-diol metabolite of DHT. The C result of the reported variant (D85Y) causes low enzyme activity leading to poor elimination of substrates. The variant is very common (50% prevelance) in Caucasian populations. Intestinal dysbiosis (microbial imbalance in your digestive tract) can cause inactivated compounds to become reactivated and rereleased into circulation. This is due to the production by bacteria of an enzyme called beta-glucuronidase. This means that substances ready for excretion can become unbound and rereleased into circulation leading to undesirably increased levels.	**AA**	The AA genotype is associated with normal (not slow) glucuronidation of substances including steroid hormones. This is positive since healthy elimination is an important part of overall health and wellbeing. If you have been on antibiotics, or have confirmed intestinal dysbiosis, probiotic support may be beneficial since dysbiosis is known to disrupt this pathway due to the production of beta-glucuronidase by gut bacteria. Foods that support glucuronidation include apples, oranges and cruciferous vegetables - all of which naturally contain calcium-D-glucarate, a substance that combats beta-glucuronidase. See the diagram and information on page 17 above for more information.



Other Important Factors Affected by Genetics

Heart & Vascular Health

Blood Clotting

Normal blood clotting (coagulation) is an important process that occurs naturally to prevent excessive bleeding after an injury. Platelets and proteins in your blood work together to stop bleeding by thickening and forming a clot over the injury. Clots are usually dissolved naturally after the injury has healed. Sometimes, however, clots form inside blood vessels without any obvious injury. This can cause narrowing of the blood vessels (atherosclerosis) and can become dangerous over time. Once a clot has formed it can travel to other parts of the body where it can cause deep vein thrombosis (DVT), heart attack, pulmonary embolism (clot in the lung) and stroke. Factors such as being obese, increased age, smoking, certain medications and genetics affect blood clotting.

Human ***Factor V Leiden (F5)***, a genetic variant mostly affecting Caucasian populations of European descent, is one of several substances in the blood that aids normal clotting. People with the **F5** variant have an increased tendency to develop blood clots. Women have a higher risk of developing clots due to the enhancing effect of oestrogen on blood clotting, but men who inherit the variant are also at risk of abnormal blood clotting. Factors that increase risk in both sexes are a sedentary lifestyle (lack of exercise), surgery, injuries, and blood type other than O.

Do you have inherited ***F5*** and increased risk of abnormal clotting? Check *page **23*** to see your result.

Cholesterol

Despite its bad reputation, cholesterol plays many vital roles in the body. It is essential for healthy cell membranes, the transport of fats between cells, cell signalling, nerve conduction and serves as the precursor (building block) to steroid hormones (androgens and oestrogen), bile acid (important for digestion) and vitamin D. Cholesterol is produced mostly in the liver and is carried through the bloodstream by various lipoproteins. Low-density lipoprotein (LDL) and very low-density lipoprotein (VLDL) are dubbed "bad" cholesterol because of their role in fatty build-ups in arteries (atherosclerosis). High-density lipoprotein (HDL) is dubbed "good" cholesterol because it helps carry LDL away from the arteries back to the liver to be broken down and removed from circulation. ***Apolipoprotein E (APOE)*** is one such lipoprotein responsible for removing "bad" cholesterol from circulation.

Some cholesterol is also obtained through the diet. Triglycerides are the most common type of fat in the body, they store excess energy from the diet and are carried through the bloodstream by VLDL. Ideally, you want to have more circulating HDL, and less LDL and triglycerides. Total cholesterol is the overall amount of circulating cholesterol in your bloodstream (HDL + LDL + VLDL /triglycerides). Therefore, knowing the ratio of HDL:LDL/triglycerides is a more important marker for health than total cholesterol alone.

Variants in the ***APOE*** gene decrease your ability to remove "bad" cholesterol . Check your status on *page **22.***

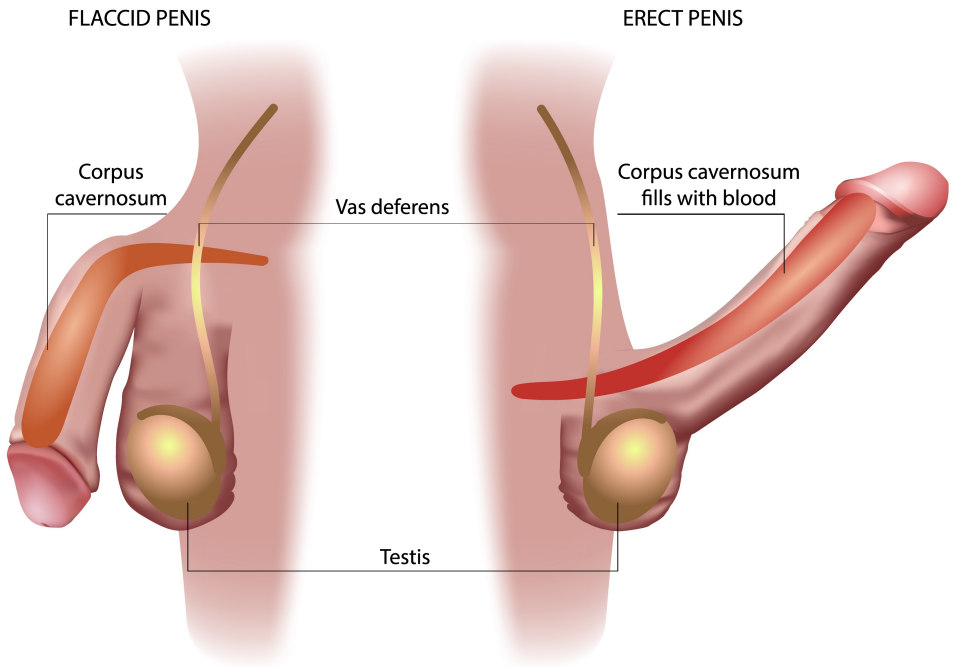
Heart & Vascular Health

Nitric Oxide

Your arteries produce nitric oxide (NO) which helps them to relax and to increase oxygen and blood flow in the body. When plaque builds up in your arteries (atherosclerosis), your capacity to produce NO reduces causing arterial stiffness and contributing to less oxygen and blood flow. For this reason low production of NO is associated with **cardiovascular disease** and also with **erectile dysfunction**. As we age, our blood vessels and NO system become less efficient due to free radical damage, inactivity, and poor diet, causing our veins and arteries to deteriorate.

The best way to increase NO production is through exercise. When you put demand on your body during exercise, your muscles need more oxygen which is supplied by the blood. As the heart pumps with more pressure, the lining in your arteries release NO into the blood, relaxing and widening the vessels. Diet is another way to increase NO production. The amino acids, **L-citrulline** and **L-arginine**, found in foods such as nuts and seeds, good quality animal meat, quinoa, dark chocolate and watermelon increase NO production. Both L-citrulline and L-arginine also help to reduce lactic acid and ammonia in muscle tissue. Beetroot, rhubarb and green leafy vegetables, particularly rocket and chard, contain **nitrates** which are eventually converted to NO.

The ***NOS3*** gene is responsible for producing the enzyme, ***nitric oxide synthase (NOS)***, which in turn is responsible for making NO in the blood vessels. Poor methylation decreases your production of NO and increases production of the free radical, **superoxide** (see page 24 for more info on methylation and superoxide).



Variants in ***NOS3*** can lead to predisposition to low *NO* production. Check your ***result*** on ***page 23.***

GENE	RESULT	IMPACT & ADVICE
APOE - Cholesterol Levels The APOE gene produces apolipoprotein E, a protein that binds and transports fats in the body. APOE is highly expressed in the liver, kidneys and brain, and is responsible for removing cholesterol, particularly "bad" (LDL and VLDL) cholesterol from the bloodstream. Variants in APOE are associated with increased total cholesterol, particularly LDL and triglycerides (a type of fat) due to decreased clearance from the body. As a result, APOE variants have been linked to high cholesterol, cardiovascular disease and also with age-related cognitive decline. High LDL cholesterol and triglycerides are often a predictor of other conditions such as obesity, high blood pressure, high blood sugar, low thyroid function and stroke. Here we report two variants (rs429358 & rs7412) in the APOE gene that are known to have an impact on function, particularly when inherited together.	**TT**	The TT genotype for this variant (rs429358) is not associated with elevated LDL cholesterol and triglyceride levels, and therefore is not linked to increased risk of atherosclerosis. Although genetically robust, poor diet and lifestyle habits such as low exercise, smoking and eating a diet high in refined, processed foods and unhealthy fats (margarine and most vegetable oils), will put you at risk of heart disease. Maintain a healthy weight by exercising regularly, watch your intake of unhealthy fats, processed foods, refined sugar and alcohol. Dietary fibre (from vegetables, beans, fruit and whole grains), and oily fish have been shown to be beneficial in lowering triglycerides.
	CC	The C result for this variant (rs7412) is associated with increased LDL cholesterol and higher triglycerides after eating. This is considered negative since it increases risk of plaque build-up in the arteries. Your risk increases further in combination with each C result for the rs429358 variant above, and decreases with a T result above. Poor diet and lifestyle choices such as lack of exercise, smoking, high alcohol intake and eating processed foods high in trans and saturated fats, will increase risk regardless of your genotype. It is particularly important that you avoid unhealthy fats such as vegetable oils, margarine and processed foods. Focus on healthy fats found in olive oil, avocados, nuts, seeds and oily fish. Maintain a healthy weight by exercising regularly.

GENE	RESULT	IMPACT & ADVICE
Factor V Leiden (F5) - Blood Clotting The T variant in this gene is fairly rare with less than 10% of the population carrying one T, and 1 in 5000 carrying two copies of T. The T variant leads to the potential to form abnormal and potentially harmful blood clots that can lead to deep vein thrombosis (DVT), heart attack, pulmonary embolism (clot in the lung) and stroke. Carrying the variant is the most common reason behind inherited thrombophilia (abnormal blood clotting), accounting for 40-50% of cases, however, not everyone with the variant will develop abnormal blood clots.	**CC**	The CC genotype is associated with normal F5 activity and decreased risk of abnormal blood clotting. Diet and lifestyle factors such as smoking, being overweight, low physical activity, testosterone therapy and a family history of clotting disorders all increase your potential for abnormal blood clotting regardless of your genotype. Regular exercise, maintaining a healthy body weight, and a diet rich in omega-3, garlic and vitamin E all help to maintain healthy blood consistency and reduce risk of abnormal clotting.
NOS3 - Nitric Oxide Production The NOS3 gene produces the enzyme nitric oxide synthase (NOS) responsible for making nitric oxide (NO). NO protects the health of blood vessels and is involved in vasodilation (opening of the blood vessels) and healthy erectile function. Variants in NOS3 result in low production of NO, increasing risk of cardiovascular disease (CVD) and erectile dysfunction (ED). Recent research shows that antioxidants, including omega-3, have a positive effect on cardiovascular risk by lowering triglycerides and increasing "good" cholesterol. The amino acids, L-citrulline and L-arginine, found in foods such as nuts and seeds, good quality animal meat, quinoa, dark chocolate and watermelon increase NO production. Beetroot, rhubarb and green leafy vegetables, particularly rocket and chard, contain nitrates which are eventually converted to NO. Here we report the D298E variant in NOS3. The T result is known to reduce NOS3 function.	**GG**	The GG genotype is associated with normal (not reduced) NOS activity and therefore healthy ability to produce NO which is positively associated with cardiovascular and erectile health. Diet and lifestyle factors such as low exercise, a poor diet, being overweight, smoking and stress may increase risk of CVD and ED regardless of your genotype. The best way to ensure and maintain CV health is to participate in regular, moderate exercise, consume a healthy diet (see pages 21 & 30 for more advice), and minimise stress as much as possible.

Healthy Ageing

Free Radicals

Free radicals are highly unstable molecules that **damage your cells**, **speed up ageing**, and **play a role in disease**. We all produce free radicals as part of normal human metabolism. We also generate, ingest, absorb and inhale them though chemicals and pesticides in our food, water, cosmetics, household cleaning products, cigarette smoke, charred foods, excessive exercise, stress, air pollution and medication.

Antioxidants help to keep free radicals in check. Vitamins A, C and E, and glutathione are all examples of powerful antioxidants derived from food that help to combat free radicals in the body. This is one of the major reasons why a healthy diet and lifestyle is so important.

Superoxide is a potent free radical produced in the body that is neutralised by the antioxidant, ***superoxide dismutase (SOD),*** produced by the ***SOD*** gene.

The ***GST*** family of enzymes are also responsible for neutralising free radicals in the body via the powerful antioxidant **glutathione.**

Your ability to neutralise free radicals is impacted by your genes which regulate the production of the ***SOD*** and ***GST*** enzymes.

Methylation

Methylation is a process that occurs in your body every second of the day. It is a vital factor for maintaining overall health and wellbeing and has many far-reaching effects. It is important for **healthy detoxification**, **maintaining DNA integrity**, **controlling gene expression** (switching genes "on" and "off"), is involved in **energy production**, **inflammation**, **immunity**, **fertility** (sperm development in men, egg and foetal development in women), **cardiovascular health** and **neurotransmitter** (brain chemical) balance.

Many factors can slow down methylation including a **poor diet, high alcohol intake, smoking, poor digestion, chemical** and **drug (especially methotrexate) exposure, physical** and **emotional stress**, and **genetic variants**. Healthy methylation relies heavily upon the availability of vital co-factors such as **B vitamins, magnesium and zinc**.

The ***MTHFR*** gene is one of the first and major genes in the methylation cycle that affects a person's ability to methylate. The primary function of ***MTHFR*** is converting folate (vitamin B9) to the active form of folate, **methylfolate**. Low production of methylfolate leads to poor down-stream methylation which has a major impact on all of the functions listed above.

Check your free radical fighting ability by reviewing your results for ***SOD2, GSTM1*** and ***GSTP1*** on *pages **25 & 27***

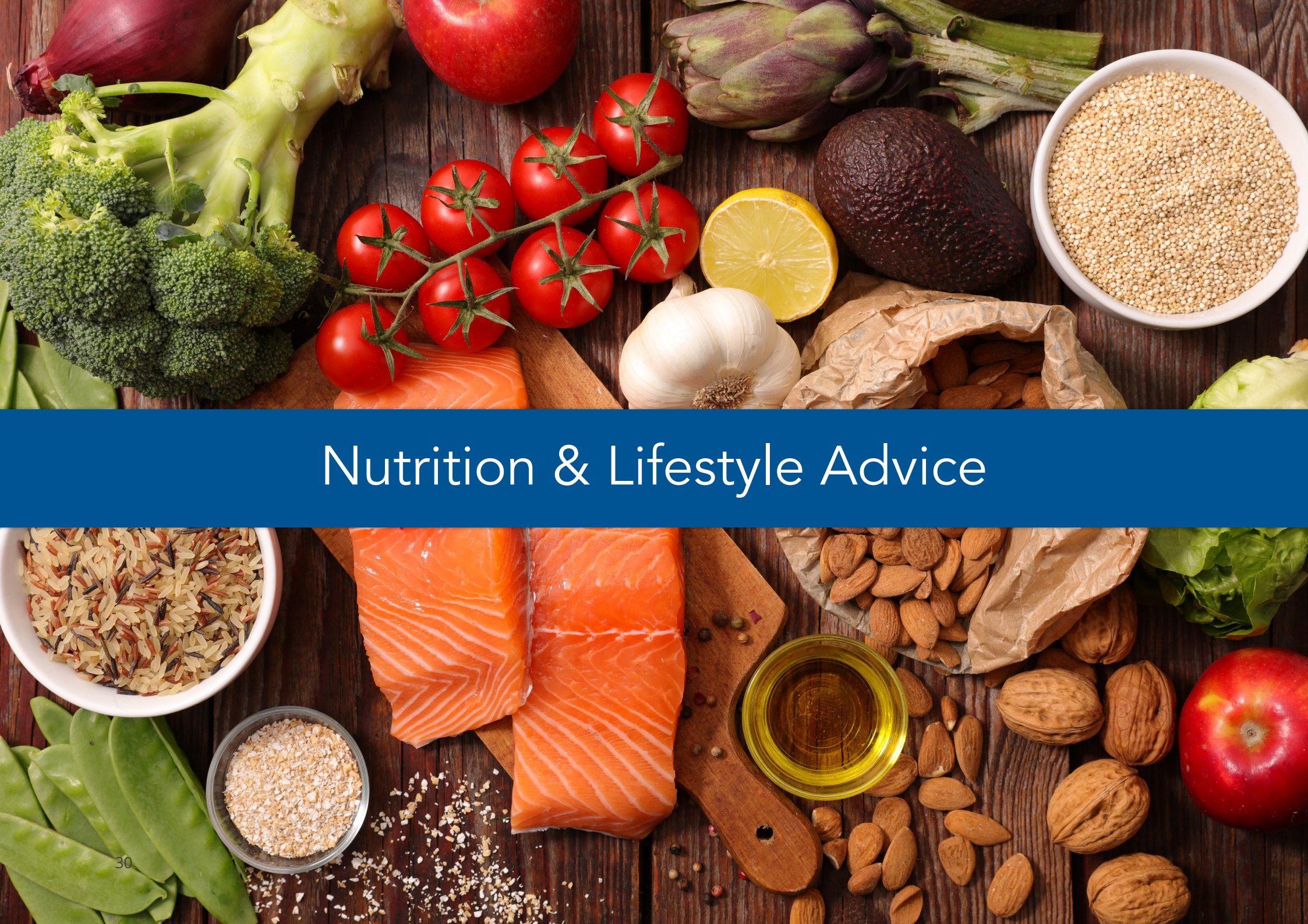
Variants in the ***MTHFR*** gene are known to reduce ability to produce active folate. Check your result on *page **26.***

GENE	RESULT	IMPACT & ADVICE
GSTM1 - Neutralising Free Radicals GSTM1 is a member of the GST superfamily of enzymes. GSTM1 is present in virtually all tissue but is most highly active in the liver, kidneys and intestines. It is responsible for neutralising compounds such as free radicals, environmental toxins, carcinogens and pharmaceutical drugs via the powerful antioxidant, glutathione (GSH). Since free radicals are known to damage DNA, GSTM1 is also involved in preventing cellular and DNA mutations. The variant in this gene is very common with approximately 50% of the population having only one (DI) or no (DD) copies of the gene at all, leading to increased susceptibility to environmental toxins and free radical damage.	**DD**	The DD genotype represents an absent GSTM1 gene. This is considered negative since GSTM1 is important for neutralising free radicals (oxidative stress), toxins and other carcinogens in the body via glutathione. High levels of oxidative stress due to poor diet and lifestyle habits such as smoking, alcohol, stress, consumption of grilled meats and exposure to chemicals in detergents or cosmetics will burden and slow down GSTM1 activity. A diet rich in antioxidants and cruciferous vegetables is recommended to help to support this pathway.
GSTP1 - Neutralising Free Radicals GSTP1 is another member of the GST superfamily of enzymes highly expressed in the liver, kidneys, oesophagus, thyroid and intestines. Its main role is to protect cells against toxins and carcinogens such as pollution, heavy metals, cigarette smoke, pesticides and UV exposure via the powerful antioxidant, glutathione (GSH). The G result of the variant reported here (I105V) is associated with impaired function. See page 24 above for more information on Free Radicals.	**GG**	The GG genotype is associated with impaired GSTP1 activity and reduced ability to neutralise free radicals. If you also have the ID or DD genotype for GSTM1 above, it is particularly important that you avoid high levels of oxidative stress caused by smoking (or second hand smoke), eating chargrilled foods, high alcohol consumption, stress and excessive exercise. Reducing stress and inflammation and increasing antioxidants is recommended to fight free radical damage. Support this pathway by eating plenty of cruciferous vegetables and 'clean' protein which will provide the raw materials for your body to produce GSH. See page 30 for more healthy diet and lifestyle recommendations.

GENE	RESULT	IMPACT & ADVICE
MTHFR - Methylation The MTHFR gene is responsible for converting folate (vitamin B9) into its active form, methylfolate. Methylfolate is an important component of methylation, a biochemical reaction involved in many processes in the body including detoxification, DNA synthesis and repair (vital for healthy cell division), gene expression, foetal development, and the metabolism of neurotransmitters, especially dopamine and serotonin. Variants in MTHFR lead to low activity and therefore low production of methylfolate. Here we report two variants on the MTHFR gene (A1298C and C677T) known to impact function. See page 24 above for more information on Methylation.	**TT**	The TT genotype in this variant (A1298C) is associated with healthy (not decreased) MTHFR activity and normal conversion of folate to active folate (methylfolate). Methylation is important for the elimination of stress hormones & oestrogen, balanced moods, healthy sperm development, cardiovascular health and gene expression. A diet rich in green leafy vegetables (B vitamins & magnesium) and low in alcohol is recommended to support healthy methylation.
	AA	'Poor Methylator'. The AA genotype in this variant (C677T) is associated with reduced MTHFR activity and lower production of active folate (methylfolate). This can lead to increased risk of methylation-dependent conditions such as imbalanced moods, poor elimination (particularly of stress hormones & oestrogen), poor sperm development and cardiovascular disease. Consume a diet rich in green leafy vegetables (B vitamins and magnesium). Low alcohol consumption is also recommended. Avoid folic acid, a synthetic form of folate added to many common foods and supplements.

GENE	RESULT	IMPACT & ADVICE
SOD2 - Antioxidant (Neutralising Free Radicals) The SOD2 gene is responsible for producing an enzyme, superoxide dismutase 2, that neutralises the harmful free radical, superoxide. Superoxide is a natural by-product of energy metabolism and can cause damage to cells and inflammation, increasing risk of disease such as certain types of cancer, liver cirrhosis and damage to brain cells, if not broken down and eliminated. Variants in the SOD2 gene cause decreased ability to break down superoxide, leading to the potential for increased free radical damage in the body. The G result of the reported variant (V16A) is associated with reduced SOD2 enzyme activity. The SOD2 enzyme requires manganese (found in pineapples, almonds, peanuts, walnuts, hazelnuts, pumpkin seeds, chia seeds, sunflower seeds, beans, spinach, green and black tea and brown rice) to function optimally. See page 24 above for more information on Free Radicals.	**GA**	The GA genotype is associated with intermediate SOD enzyme activity and therefore a slightly reduced ability to break down the harmful superoxide free radical. This genotype has also been linked to the development of cirrhosis of the liver in heavy drinkers due to poor protection from oxidative stress (high amounts of free radicals which cause damage to the body). Eat a varied diet rich in manganese foods (listed left) and antioxidants such as vitamins A, C and E. Avoid smoking, heavy drinking, excessive exercise, environmental and dietary chemicals (opt for organic produce where possible) and sunburn to minimise free radical damage in the body.

GENE	RESULT	IMPACT & ADVICE
VDR - Vitamin D Receptivity The VDR gene regulates the body's receptivity to vitamin D3, the active form of vitamin D. This vitamin can be acquired from certain foods but is mostly manufactured in the body following exposure to sunlight. Vitamin D serves many important functions in the body: it aids in the absorption of calcium and phosphate - keeping bones and teeth healthy; it mediates the production of dopamine (a 'feel good' chemical) - this is one of the reasons why lack of sunlight is associated with low mood; it is also crucial for cell growth and differentiation, and supports a healthy immune system. Low vitamin D levels have been linked to reduced testosterone levels, poor bone health, depression, inflammation, frequent infections and autoimmune conditions. Over 30% of the population carry genetic variants that cause low vitamin D receptivity. Here we report two variants (Bsml and Taql) on the VDR gene which are known to reduce receptivity.	**CC**	The CC genotype in Bsml is associated with healthy (not reduced) vitamin D receptivity. Provided you have adequate daily sunlight exposure (without tanning or burning your skin), or take a good quality vitamin D supplement, you are less likely to have low vitamin D levels and therefore lower risk of fragile bones, low mood, decreased testosterone levels, and poor immunity. Consume foods rich in vitamin D including fatty fish, beef liver, egg yolk and mushrooms.
	AA	The AA genotype in Taql is associated with normal (not reduced) vitamin D3 receptor activity. Provided you have adequate daily sunlight exposure without tanning or burning your skin, or take a good quality vitamin D supplement, you are less likely to experience symptoms associated with low vitamin D levels such as fragile bones, low mood, reduced testosterone levels, and poor immunity. Your need for vitamin D increases if you have a T result for the BsmI SNP above. Consume foods rich in vitamin D including fatty fish, beef liver, egg yolk and mushrooms.



Nutrition & Lifestyle Advice

Reduce / Eliminate

Tight Underwear, Trauma & Heat

The majority of your testosterone and all of your sperm is made in your testicles - be kind to them! Avoid wearing underwear that restricts healthy blood flow. Protect them when playing physical sport or cycling. Although saunas are great for improving circulation and detoxification, the heat isn't good for sperm production so if you are trying to conceive, you might want to skip them for a while

Unhealthy Foods

Processed, grilled & smoked meats: such as sandwich meat, bacon, sausages etc. which contain substances known to be carcinogenic and bad for cardiovascular (heart) health

Simple carbs: white bread, pasta and rice, most boxed breakfast cereals, most sodas and energy drinks. These can lead to blood sugar spikes and high insulin which disrupt hormones and increase fat storage

Alcohol & caffeine: both are pro-inflammatory and reduce the absorption of many vitamins and minerals. Alcohol decreases sperm production

Stress

One of the first things to take a hit when you are stressed is your sex drive. This is because high stress is a major cause of low testosterone levels. Over time, the negative effects of chronic stress are far reaching. Make sure you address stress as early as possible. Exercise, meditate, hike, cut caffeine, socialise with friends, change jobs, see a therapist - find something that works for you!

Smoking & Toxic Chemicals

(plastics, pesticides, pollution, cosmetics, household detergents etc.)

These disrupt hormones, mainly by decreasing testosterone and increasing oestrogen; generate free radicals in the body and place high demand on your liver which slows detoxification

Increase

Regular Exercise (at least 30 mins/day)

Being physically fit improves overall health and well-being and reduces risk of disease. Exercise helps to maintain healthy testosterone levels, relieves stress, depression and anxiety, and improves sleep quality. Since adipose (fat) tissue produces oestrogen, decreasing body fat and maintaining a healthy weight is important for balanced hormone levels. A mixture of aerobic and strength training is best

Health Promoting Foods

'Clean' protein: nuts, seeds, beans, organic, free-range eggs & meat, and wild caught fish

Complex carbs: whole grains (e.g. buckwheat, quinoa, brown rice, oatmeal etc.) beans, carrots, sweet potato, parsnips, pumpkin and swede

Healthy fats: extra virgin olive oil, pumpkin seed oil, avocados, coconut oil, nuts, seeds and fatty fish

Fruit & veg: cruciferous vegetables (broccoli, cabbage, cauliflower, Brussels sprouts, cress, horseradish, kale, bok choy, rocket etc.), beetroot, spinach, radish, tomatoes, apples, berries, bananas, pears and oranges

Herbs & spices: saw palmetto, nettle, ashwagandha

Sleep

One of the best and easiest ways to reduce stress and increase testosterone levels is good, refreshing sleep. Aim for 7-9h / night when possible. Create a regular sleep / wake routine. Make sure your bedroom is dark, cool, quiet and comfortable. Avoid bright lights, heavy meals and screens in the evening. Rather read a book before bed

Herbal Teas & Filtered Water

Green tea, maca, rooibos, peppermint, dandelion, nettle, ginseng; and filtered water help to keep your kidneys and liver working well, supporting detoxification and hormone balance