

Male Health Genetic Report

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## Gene Contents

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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
<b>GENE CODE - Gene Function</b> Explanation of the role the gene plays and what effect genetic variants might have, symptoms, other contributing factors.	AG	An explanation of your result, how you might be affected along with specific diet and lifestyle advice
<b>GENE CODE - Gene Function</b> Explanation of the role the gene plays and what effect genetic variants might have, symptoms, other contributing factors.	AA	An explanation of your result, how you might be affected along with specific diet and lifestyle advice

### Testosterone

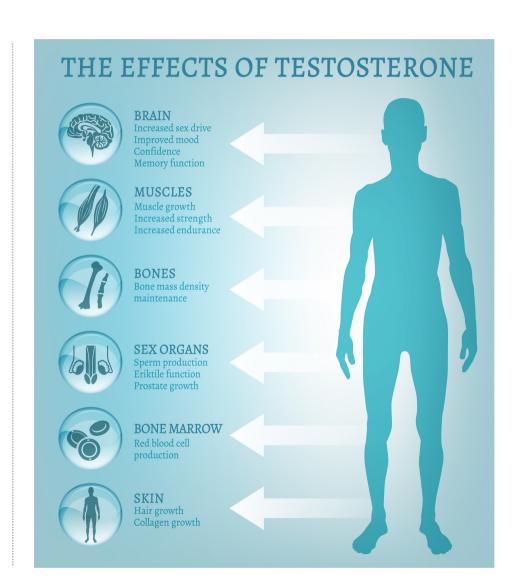
**Testosterone** is the main steroid hormone (androgen) in men responsible for sex drive, enlargement of the penis, sperm production & development, increased muscle mass, fat distribution, red blood cell production and lowering of the voice. Most of the testosterone in men is produced in the testes,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

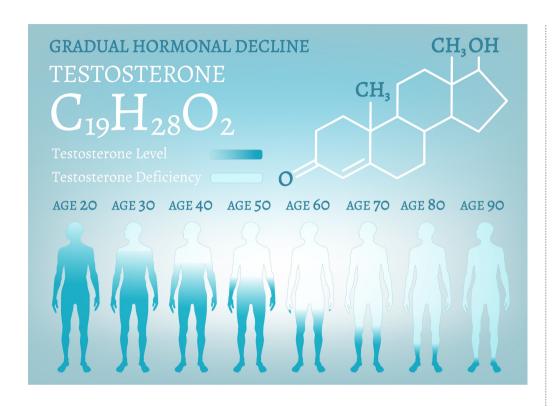
Once produced, testosterone is bound and transported in the blood by the protein, **sex hormone binding globulin (SHBG)** and, to a lesser extent, by albumin. To become active, testosterone must be released from SHBG and bind to **androgen receptors (ARs)** in target tissues.

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

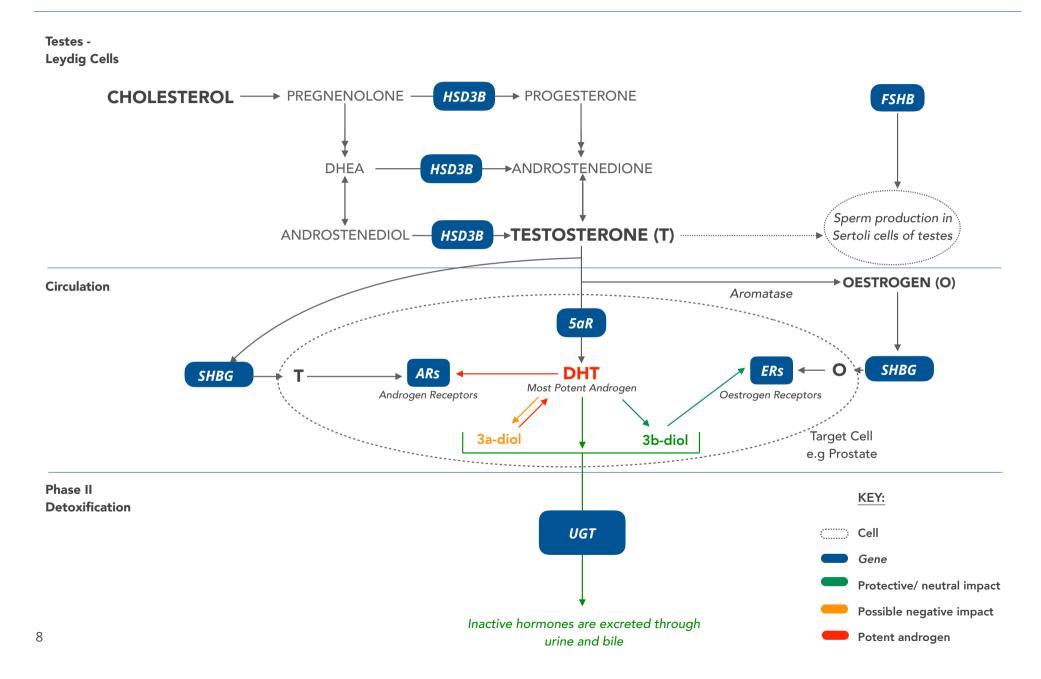
Maintaining a healthy testosterone level is extremely important for overall health and well-being in men. Both high and low testosterone can have a negative impact. Healthy males make about 3-10mg of testosterone per day.

### 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

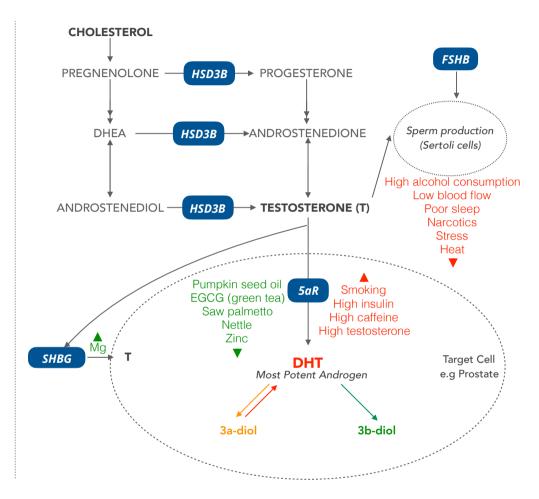


# Androgen Production

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).
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.	TT	The TT genotype is more common in African populations and is associated with increased systemic DHT levels. This is undesirable since high levels of DHT can increase risk of androgen-linked conditions such as hair loss and enlarged prostate (see left for more). The C result for the HSDß1 variant above, increases likelihood of high DHT levels. Check your results for 5aR1 & 5aR2 on page 12 below and follow the advice given for ways to naturally reduce DHT.

GENE	RESULT	IMPACT & ADVICE
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.	GA	The GA genotype is associated with increased SHBG levels, increased total testosterone (tT) and decreased free testosterone (fT) levels. Since bound testosterone is inactive, this could result in symptoms of low testosterone. See page 7 above for a list of symptoms, and of other factors that can contribute to low (and high) testosterone levels. Magnesium helps to release T from SHBG and may be helpful in naturally raising low levels of fT. Consider having your SHBG levels tested if you experience more than one of the symptoms reported on page 7.
<b>5aR1 - Testosterone to DHT (Serum)</b> 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.	GA	The TC genotype is associated with increased 5aR1 activity and higher serum DHT levels. This is negative because high DHT levels have been associated with androgen-linked conditions such as hair loss and enlarged prostate gland. Risk increases with a high-activity androgen receptor (AR) result, see pages 13 & 14. Smoking, high caffeine intake and high insulin levels increase 5aR activity further. Specific substances that naturally reduce 5aR activity include pumpkin seed oil, green tea, saw palmetto, nettle and zinc.

GENE	RESULT	IMPACT & ADVICE
<b>5aR2 - Testosterone to DHT (Target cells, particularly prostate)</b> 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.	GC	The GC genotype of this V89L variant is associated with less active 5aR2 and therefore predisposition to lower 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.
	TΤ	The TT genotype of this A49T variant is linked to an increased conversion of testosterone to DHT. This is negative because DHT has been shown to increase risk of androgen-dependent conditions such as male pattern balding and benign prostatic hyperplasia (BPH). Risk increases if you have the high-activity variant on AR (see pages 13 & 14 below). Smoking, high caffeine intake and high insulin levels increase 5aR activity further. Specific substances that help to naturally reduce 5aR activity include pumpkin seed oil, green tea, saw palmetto, nettle and zinc.