# DNA*pal*

## Thyroid Genetic Panel

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## Gene List

# Understanding your genetic report

## What is DNA?

DNA is your body's instruction manual, controlling every single function from when you were only made up of a few cells, until now. It looks like a twisted ladder, made up of two halves - you inherit one half from your mother, the other from your father. This combination is what makes you, you.

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 which use combinations of the contained code to perform specific functions.

## SNPs

Over time, due to environmental and lifestyle shifts, minor changes called **single nucleotide polymorphisms (SNPs)** occur in 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 instructions given to a gene.

Some changes are positive, making us stronger and more resilient (like being able to digest milk after infancy), some 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 on just one side of your ladder, from one parent, or from both, enhancing the effect. They 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 the result is potentially good, neutral or less favourable.

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

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

An amber result usually indicates one genetic variant present, and thus potentially a mildly negative impact

A red result indicates a potentially 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**<br>Explanation of the role the gene plays and what effect genetic variants might have, symptoms etc. | TT | An explanation of your result, how you might be affected along with diet and lifestyle advice |
| **GENE CODE - Gene Function**<br>Explanation of the role the gene plays and what effect genetic variants might have, symptoms etc. | CT | An explanation of your result, how you might be affected along with diet and lifestyle advice |
| **GENE CODE - Gene Function**<br>Explanation of the role the gene plays and what effect genetic variants might have, symptoms etc. | CC | An explanation of your result, how you might be affected along with diet and lifestyle advice |

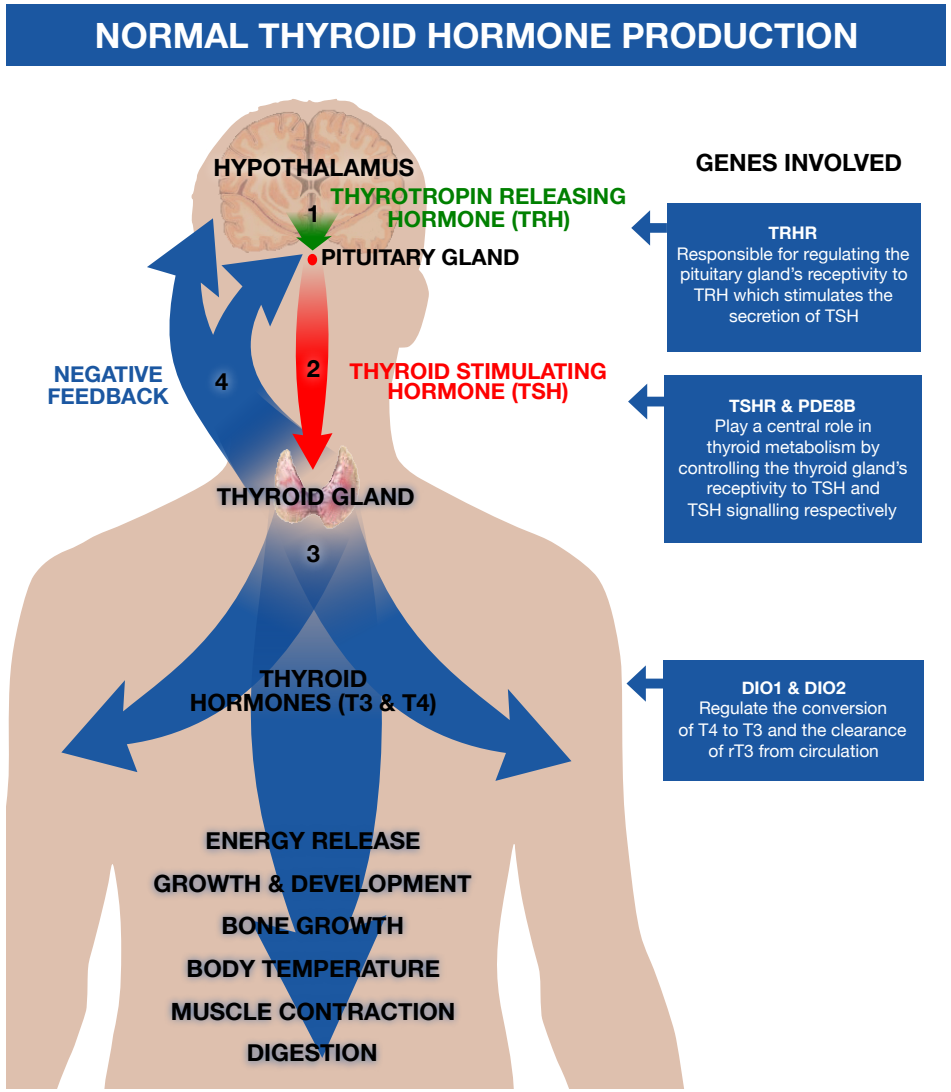
# Thyroid Function

Your thyroid gland is responsible for regulating a number of bodily functions, including your metabolism (energy production), body temperature, growth and repair, muscle contraction and digestion processes. The thyroid cells are the only cells in the body which can absorb iodine. They combine iodine with the amino acid tyrosine to produce two main thyroid hormones: **thyroxine (T4)** and its active counterpart, **triiodothyronine (T3),** which are then released into the blood stream.

T3 is critical to making every system in your body work at the right speed. Although T3 is the more active thyroid hormone, the thyroid gland produces much more T4 than T3. T4 is converted to T3 when needed. Too much T3 will cause enzymes to convert it into reverse T3 (rT3), an inactive form. If you produce too much or too little thyroid hormone, your whole body will be affected. Balance is key.

Thyroid hormone balance is maintained via negative feedback. When thyroid hormone levels fall too low, (1) the hypothalamus (in the brain) produces **thyrotropin releasing hormone (TRH)** which stimulates the pituitary gland (also in the brain) to (2) release **thyroid stimulating hormone (TSH)**. TSH stimulates the thyroid to (3) produce more thyroid hormones (T4 and T3). As soon as levels increase again, the pituitary responds by (4) decreasing production of TSH.

Genes play a vital role in regulating this mechanism. Studies into genetic inheritance suggest that up to 67% of circulating TSH and thyroid hormone levels are genetically determined (Panicker, 2011).



# Thyroid Disorders

**Hypothyroidism (underactive thyroid)**

This occurs when the thyroid gland produces too little thyroid hormone. Symptoms include persistent fatigue, moodiness, depression and anxiety, dry hair and skin, puffy face, brain fog, hoarse voice, weight gain, constipation, muscle weakness, aches and pains, sensitivity to cold, heavy periods, thinning hair and loss of outer eyebrow hair. Thyroid function blood test results usually show elevated TSH along with low T4 and T3.

**Hashimoto's Thyroiditis (HT)**

"Hashimoto's" is an autoimmune condition and is one of the most common causes of hypothyroidism. Autoimmune disorders occur when your immune system produces antibodies that attack your own tissues. In this case, the thyroid gland, and the antibodies cause it to function poorly. HT has a genetic link and tends to run in families. Test results usually show high levels of thyroid peroxidase antibodies (TPOAb) in particular, and possibly thyroglobulin antibodies (TGAb).

**Hyperthyroidism (overactive thyroid)**

This is the situation when the thyroid gland produces too much thyroid hormone. Symptoms include nervousness, insomnia, racing heart, bulging eyes, unexplained weight loss, sweating, muscle weakness, frequent bowel movements, thin and brittle hair, intolerance to heat, fine tremor of hands or fingers, enlargement of the thyroid gland (goiter), changes in menstrual cycle, erectile dysfunction or reduced libido. Lab results usually show extremely low TSH with elevated FT4 and FT3.

**Graves' Disease (GD)**

GD is the most common cause of overactive thyroid. Like Hashimoto's, it is also an autoimmune disease, however, unlike Hashimoto's, Graves' causes the thyroid to over-secrete thyroid hormones. This type of hyperthyroidism also tends to run in families and occurs more often in young women. The most noticeable symptom of Graves' Disease is a condition known as Graves' opthalmopathy, an inflammation of the eyes and swelling of the tissue behind the eye that causes them to bulge. Thyroid function blood results will usually reveal TPOAb and/or TGAb.

**Secondary Hypo or Hyperthyroidism**

Secondary hypothyroidism or hyperthyroidism occurs when a dysfunction of the hypothalamus or pituitary gland causes the thyroid to under or over produce thyroid hormones - by under or over secreting TSH. Thyroid function tests will generally show low TSH, T4 & T3 or high TSH, T4 & T3 respectively.

# Thyroid Disruptors

### Stress

Cortisol is an essential hormone produced by the adrenal glands (located near the kidneys), with many functions - it is released in small amounts to promote wakefulness and in larger amounts in response to physical and emotional stress. High cortisol levels lower TSH, reduce the conversion of T4 to T3, and increase inactive rT3. Since T3 and rT3 compete for binding sites in cells, high rT3 may make remaining T3 even less effective.

### Inflammation & infection

Prolonged inflammation, due to infection or persistent irritation, causes the body to convert T4 to inactive rT3 and may reduce the body's receptivity to thyroid hormones, creating symptoms of hypothyroidism (even though standard thyroid function results for TSH, T4 and T3 might be normal). Chronic inflammation is also linked to the development of autoimmune conditions, such as Hashimoto's and Graves' diseases.

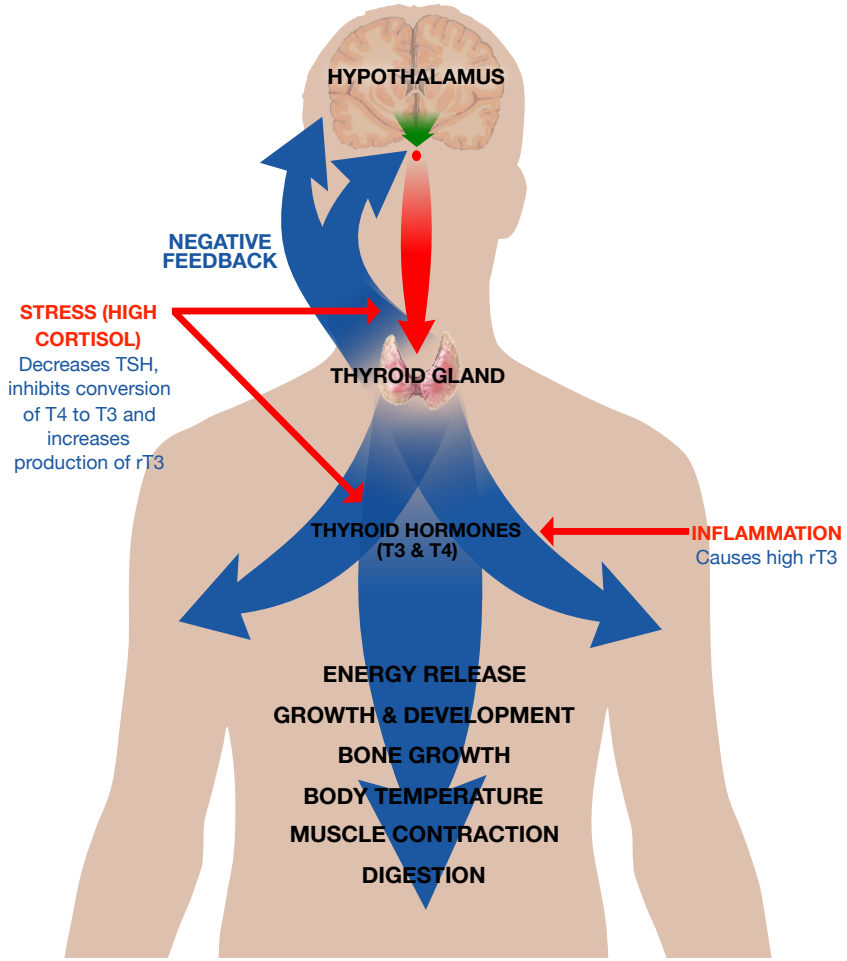
### Lack of key nutrients

Iodine and tyrosine are required components of thyroid hormones. Iron is important for the production of thyroid hormones too, and low levels are associated with hypothyroidism. Selenium and zinc are important for the conversion of T4 to T3. Selenium deficiency results in increased production of rT3, and zinc is also vital for the hypothalamus to respond to low circulating thyroid hormone levels. Vitamin D may have a protective effect against the development of autoimmune diseases, as well as osteoporosis (a result of long term hyperthyroidism). Vitamin A aids TSH production in the pituitary gland.

### Genetics

Recent evidence suggests that genetic factors are likely to play a major role in thyroid function and that this accounts for roughly 50% of the variations seen between individuals in serum thyroid levels (Medici et al, 2015)

## THYROID FUNCTION DISRUPTORS




**GENETIC VARIANTS**

Variations in the genes involved in thyroid metabolism and in stress and inflammation in the body have an effect on thyroid function, thyroid hormone levels and the body's receptivity to circulating thyroid hormones

**LOW LEVELS OF KEY NUTRIENTS**

- Iodine
- Tyrosine
- Selenium
- Iron
- Zinc
- Vitamin A
- Vitamin C
- Vitamin D

# Your thyroid genotype and advice:

| GENE | RESULT | IMPACT & ADVICE |
|---|---|---|
| **COMT - Inactivation of Stress Hormones and Oestrogen**<br>COMT is one of the main inactivating enzymes of stress hormones and oestrogen in the body. COMT variants cause slow clearance of stress hormones and oestrogen leading to high oestrogen and stress hormone levels which may also be linked to thyroid hormone dysfunction. | **GG** | The G allele on rs4680 is associated with healthy clearance of stress hormones and oestrogen from the body. You are therefore less likely to experience thyroid dysfunction as a result of high circulating hormones known to have a negative impact. |
| **DIO1 - Thyroid Hormone Activation**<br>"D1" is largely expressed in the liver and kidneys. It is responsible for the clearance of rT3 from circulation, and for facilitating the conversion of T4 to T3 in plasma and surrounding tissue. This process requires selenium and iodine for optimum function. Here we look at two variants linked to poor conversion of T4 to T3 and reduced clearance of rT3. | **AA** | The A allele on rs2235544 is associated with normal (not increased) DIO1 activity and therefore normal (not increased) conversion of FT4 to T3, or clearance of circulating rT3 levels. This is not as desirable as inheriting the C allele which causes increased DIO1 activity. Ensure adequate iodine and selenium intake to support this pathway optimally. |
| | **TC** | The T allele on rs11206244 is associated with lower DIO1 activity and therefore likely decreased clearance of rT3 from circulation, and lower conversion of T4 to T3. Ensure adequate intake of iodine and selenium to support this pathway. |

# Your thyroid genotype and advice:

| GENE | RESULT | IMPACT & ADVICE |
|---|---|---|
| **DIO2 - Thyroid Hormone Activation**<br>"D2" is importantly expressed in the central nervous system, pituitary, brown fat tissue and muscle, and responds to changes in thyroid levels. D2 is responsible for the 'local' conversion of T4 to T3 in the thyroid, placenta and brain. It requires selenium and iodine to function optimally. Here we look at two different variants linked to decreased T4 and low mood in certain individuals. | CC | The C allele on rs225014 is associated with anxiety and depression in many cases in those taking thyroxine (T4) hormone replacement therapy for hypothyroidism. This can be overcome by taking combined T4/T3 therapy. Ensure adequate nutrition for bone health, such as calcium, and vitamin D (which may also help with low mood). |
| | TC | The T allele on rs12885300 is associated with increased DIO2 activity. This has been shown to present as lower T4 and rT3, and higher T3 levels which is positive. Adequate levels of iodine and selenium are required for optimal functioning of this pathway. |
| **FKBP5 - Cortisol Regulation**<br>FKBP5 is an important stress-regulating gene responsible for lowering cortisol levels after a stress response. Variants are associated with prolonged and increased symptoms of stress, which may be due to delayed lowering of cortisol levels. | CC | The C allele on rs1360780 is associated with healthy cortisol regulation and stress resilience. You are likely to be less negatively affected by stress and the impact it has on the body. Thyroid hormone regulation is likely to be less affected also. |
| **PDE8B - TSH Signalling**<br>PDE8B is found in the thyroid but not the pituitary, and is involved in TSH signalling. It is thought that the variant decreases the response of the thyroid gland to TSH stimulation. | AA | The A allele on rs4704397 is linked to reduced thyroid sensitivity to TSH stimulation. This could result in higher TSH levels in order to produce normal levels of thyroid hormones (T4 and T3). A clinical test would show high TSH levels and normal to low thyroid hormones. |

# Your thyroid genotype and advice:

| GENE | RESULT | IMPACT & ADVICE |
|---|---|---|
| **TNF-a - Inflammation**<br>TNF-a is an inflammatory cytokine that helps regulate the immune reaction involved in inflammation, giving rise to fever and inhibiting tumour growth. If poorly controlled, it may be implicated in a number of autoimmune disorders. Variants in TNF-a are associated with overreactive immune responses and prolonged inflammation. | AG | The A allele on rs1800629 increases likelihood of an overreactive inflammatory immune responses. This means you are at increased risk of chronic inflammatory and autoimmune conditions, including Hashimoto's thyroiditis or Graves' disease. It is important for you to minimise stress, and follow a healthy diet and exercise regime to manage risk. |
| **TSHR - Thyroid Stimulating Hormone (TSH) Receptor**<br>The TSHR gene plays a central role in thyroid metabolism by controlling the thyroid gland's receptivity to TSH. Variants in this gene have been linked to hyperthyroidism, particularly to Graves' Disease (GD). | AA | The A allele on rs179247 has been linked to the presence of thyroid stimulating hormone receptor antibodies (TRAb), associated with increased risk of developing Graves' Disease (GD). GD is a form of hyperthyroidism, the most common symptom being bulging eyes. Consult your GP and get tested for TRAb if you suspect you may have GD. |
| **TRHR - Thyrotropin Releasing Hormone (TRH) Receptor**<br>Responsible for the body's receptivity to TRH which stimulates the secretion of TSH from the pituitary gland. In turn, TSH stimulates the production of thyroid hormones from the thyroid gland. TRH is an important part of the negative feedback loop that ultimately regulates thyroid hormone levels. Variants have been shown to affect TSH levels. | AG | The A allele on rs3134105 is associated with a more responsive negative feedback mechanism, leading to lower circulating TSH:T3/4 ratio due to proper reduction of TRH and TSH in the presence of healthy thyroid hormone levels. This implies a reactive loop, and more effective control of thyroid hormone status. |

## Nutrients for Hypothyroidism

- ✅ ***Iodine:*** sea vegetables (kelp, nori, wakame), ocean fish, iodised salt, yoghurt
- ✅ ***Tyrosine (protein):*** eggs, meat, beans, seeds, cheese
- ✅ ***Selenium:*** Brazil nuts, spinach, sardines, turkey, beef liver
- ✅ ***Iron:*** liver, animal meat, seafood
- ✅ ***Zinc:*** wild-caught salmon, organic organ meat, pumpkin & chia seeds, almonds, oysters
- ✅ ***Magnesium:*** spinach, chard, pumpkin seeds
- ✅ ***Vitamin A:*** Cod liver oil, carrots, sweet potatoes, dark green leafy veg
- ✅ ***Vitamin D:*** Seafood, liver, eggs, mushrooms and sunshine!
- ❌ ***Fluoride:*** depletes iodine
- ❌ ***Soy:*** large amounts block TH absorption

## Nutrients for Hyperthyroidism

- ✅ ***B Complex:*** particularly B1 & B6
- ✅ ***Vitamin C:*** berries, citrus fruit, papaya, bell peppers, guava, kiwi
- ✅ ***Vitamin D:*** Seafood, liver, eggs, mushrooms and sunshine!
- ✅ ***Vitamin E:*** almonds, spinach, avocado, sunflower seeds
- ✅ ***Calcium:*** spinach, kale, white beans, bony fish
- ✅ ***Antioxidants:*** berries, turmeric, dark chocolate
- ✅ ***Omega-3:*** Oily fish, egg yolks, cod liver oil, seeds
- ✅ ***L-carnitine:*** Beef, chicken, cheddar (if not dairy-intolerant), asparagus
- ✅ ***Probiotics:*** healthy gut bacteria may help with the elimination of excess circulating TH
- ❌ ***Suspected food allergens*** such as dairy, gluten, soy and chemical food additives
- ❌ ***Iodine***

## Lifestyle Recommendations

- ✅ ***Stress management:*** make time for relaxation and to do things you enjoy
- ✅ ***Exercise:*** Improves cellular sensitivity to thyroid hormones. Aim for at least 30 mins, 5 days a week
- ✅ ***Sleep:*** Adequate sleep helps to balance thyroid hormones. Aim for 7-9 hrs a night. Keep a routine, switch off all electronics 2 hours before bed
- ❌ ***Alcohol:*** drink in moderation. Alcohol has been shown to suppress thyroid function and can block absorption of vital nutrients
- ❌ ***Smoking:*** bad for health in general and is a risk factor for Graves' Disease
- ❌ ***Caffeine:*** caffeine increases cortisol production, consume in moderation. If taking thyroid medication, wait at least 60 minutes before drinking tea or coffee (blocks absorption)