Lifecode GX ®
— Professional Genotype Analysis —

Hormones Report

A hormone is a signalling molecule that is made by specialist cells, usually within an endocrine gland.

The body produces more than 50 hormones to control and coordinate metabolism, energy level, reproduction, growth & development, and response to injury, stress, and environmental factors. Hormones are produced in different organs and tissues, and have broad functions. There are three classes of hormones - steroid hormones (corticosteroids and sex steroids), amines (present in the Nervous System Report), and proteins and peptides.

The focus of this report is mainly steroid hormones, plus adrenaline, insulin and melatonin. Steroid hormone imbalances can have serious physical and mental health effects. Symptoms and consequences of steroid hormone imbalances include fertility issues, PCOS (polycystic ovary syndrome), endometriosis, menstrual irregularities, excess facial hair (for women) or breast tissue (for men), osteoporosis, heart disease, blood clots, acne, sexual dysfunction, low libido, mood swings, poor memory, weight gain and hormone sensitive cancers.

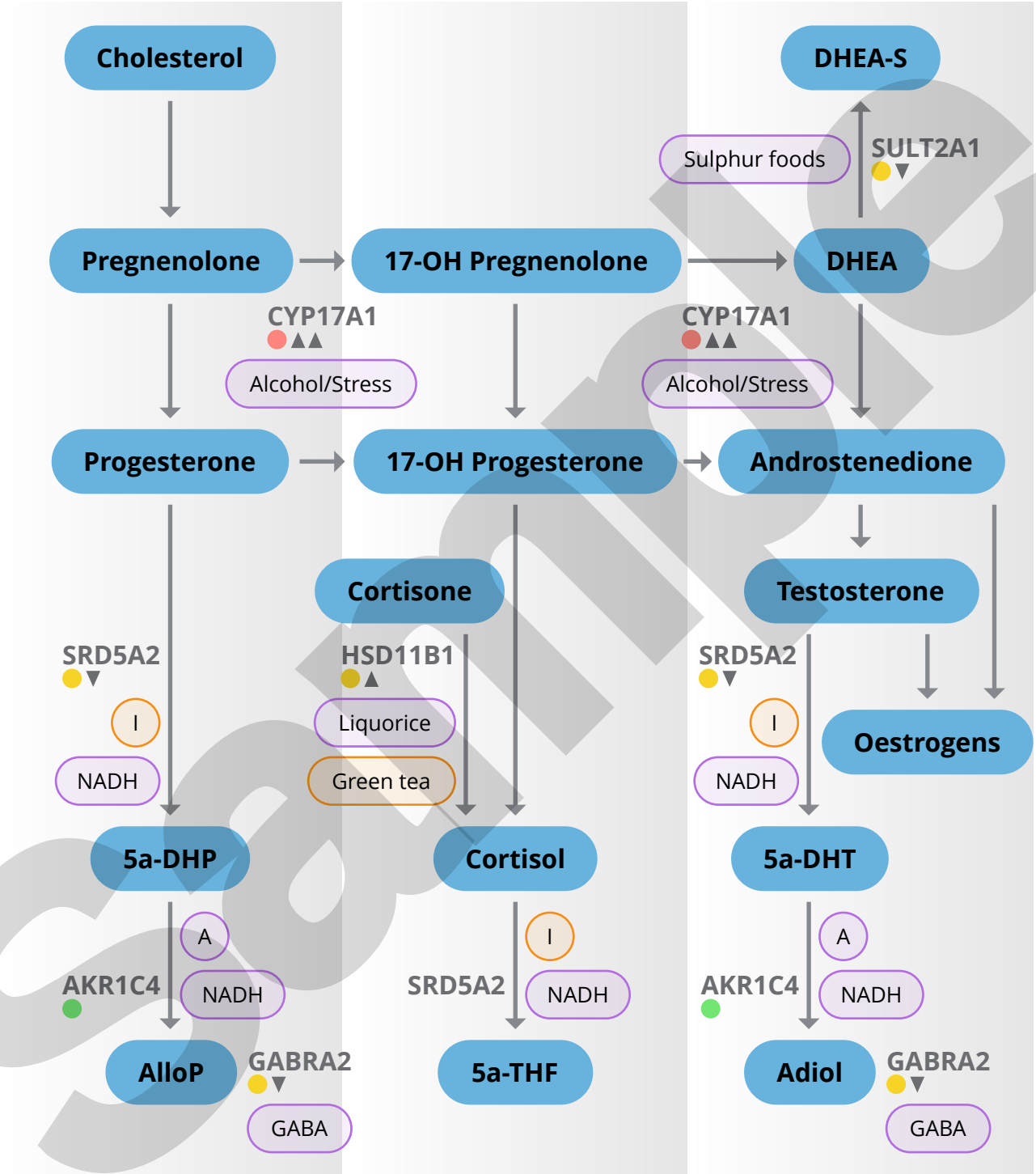
Steroid hormone activity is altered by genetics and environmental factors. Insufficiency or excess can result in HP-GA axis (Hypothalamus-Pituitary-Gonads/Adrenal) dysfunction, which, in turn, can impact synthesis, activation, response and metabolism of these hormones.

This report describes the genes, nutrients, and lifestyle and environmental factors that can impact steroid hormones.

It provides three personalised summary pathways and detailed results, followed by a generic steroid hormones guide. The hormones and pathways covered are:

- Steroid Hormones
- Oestrogen Lifecycle
- HPA and HPG Axis

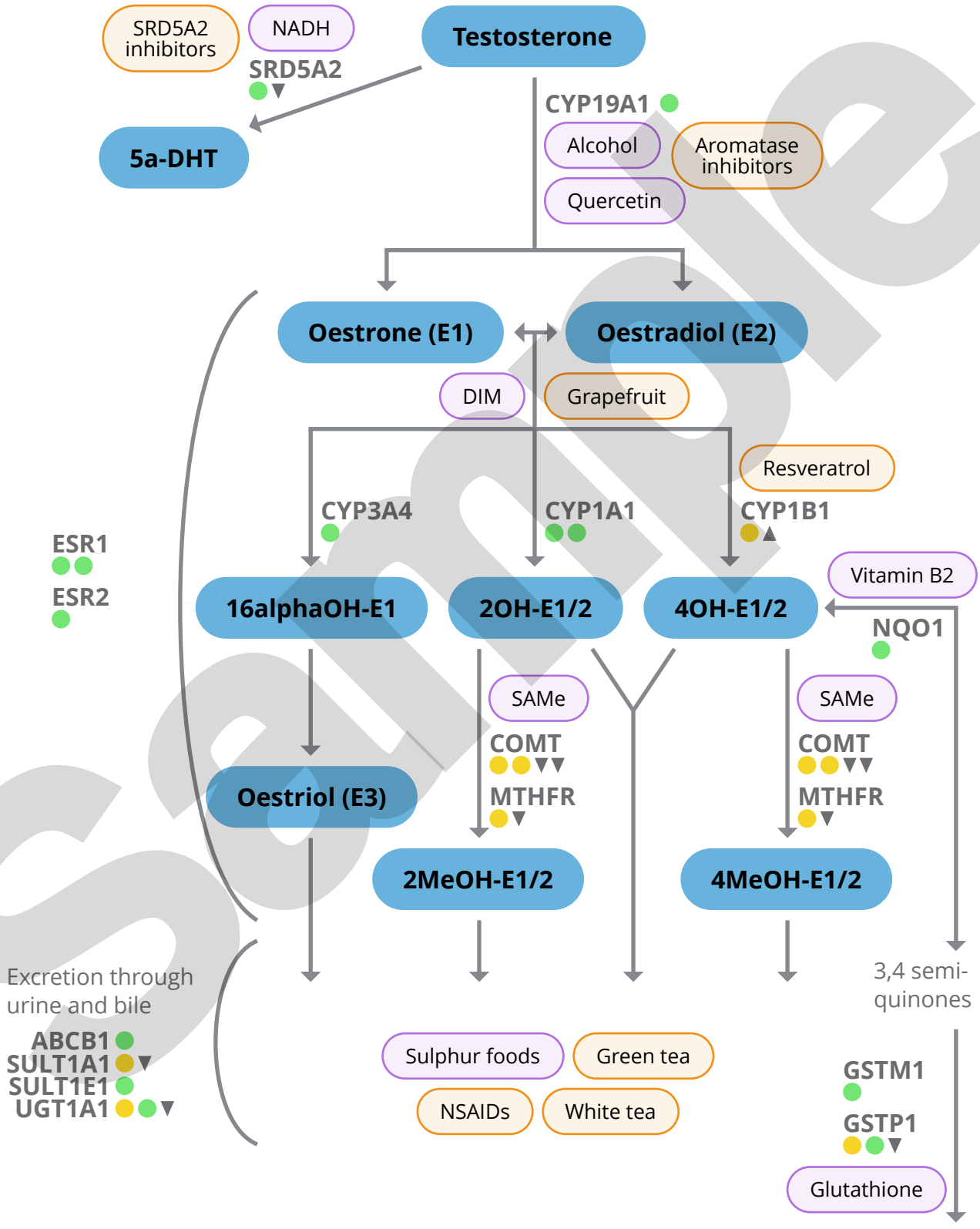
Steroid Hormones



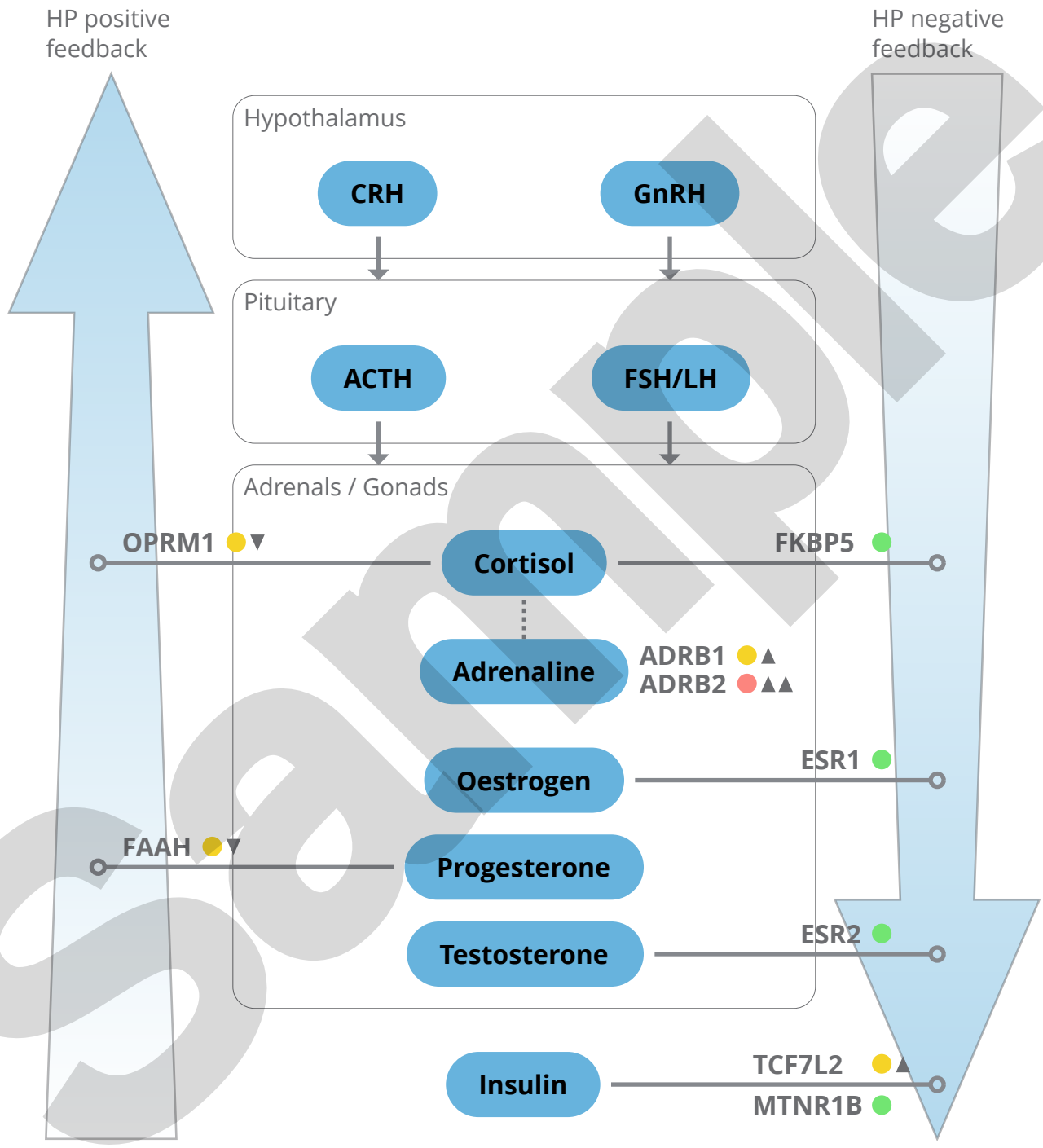
A **3a-HSD activators** include calcium, omega 3-fatty acids in particular palmitoylethanolamide (PEA), evening primrose oil, gingko biloba, crocus sativus and SSRIs.

I **5aR inhibitors** include saw palmetto, stinging nettle, quercetin, zinc, flaxseed, EGCG (epigallocatechin gallate), soy isoflavones, and medications.

Oestrogen Lifecycle



HPA and HPG Axis



If HPA response is blunted, support with Vitamin C, B vitamins and liquorice. Beware of dependency on alcohol and caffeine.

If HPA is overactive, support with anti-inflammatory foods and stress management techniques. Beware of disrupted sleep patterns and limit consumption of simple carbohydrates.

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Detailed Results for Oestrogen Lifecycle

ABCB1 rs1045642	GG	High ABCB1 enzyme activity, also known as MDRP1 (multidrug resistance protein 1 or P-glycoprotein) due to differential transport of drugs into/ out of cells thereby impacting their efficacy or toxicity. Effective transport of substrates across cellular membranes, and more effective detoxification. However, efficacy of certain pharmaceutical drugs may be compromised. Always refer to your GP or specialist before adjusting dosage of any prescribed medication.
COMT	TC ▼	Reduced COMT activity leading to less efficient inactivation of oestrogen via methylation. Poor methylation will further impede COMT activity due to low availability of cofactor SAMe. Review your MTHFR result to assess methyl need. A diet rich in B vitamins will help to improve methylation in general.
COMT	AG ▼	Reduced COMT activity leading to less efficient inactivation of oestrogen via methylation. Poor methylation will further impede COMT activity due to low availability of cofactor SAMe. Review your MTHFR result to assess methyl need. A diet rich in B vitamins will help to improve methylation in general.
CYP19A1	GG	Normal conversion of androgens to oestrogens. Diet and lifestyle factors such as inflammation, excess adipose tissue, high insulin levels and stress will increase CYP19A1 activity regardless of genotype. Maintaining a healthy weight, balancing blood sugar, reducing inflammation and stress will help balance CYP19A1 activity. Vitamin D is required for the proper functioning of CYP19A1.
CYP1A1	TT	Normal CYP1A1 enzyme activity and normal hydroxylation of oestrogens to 2OH oestrogens. Ensure phase II detoxification pathways are working optimally since increasing phase I enzymes can increase the production of free radicals. Consider antioxidants to neutralise free radicals.
CYP1A1	AA	Normal CYP1A1 enzyme activity. Not associated with increased susceptibility to PCOS. Care should be taken to improve phase II detoxification.

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A Guide to the Steroid Hormones

This guide contains detailed explanations of the hormones and genes involved in steroid hormones lifecycle and regulation.

Steroid hormones are a group of hormones derived from cholesterol that act as chemical messengers in the body. They are involved in the regulation of many physiological processes, such as the development and function of the reproductive system, metabolism, inflammation and immune system.

Steroid hormones exert their action through their receptors. They have been classified into two classes: corticosteroids (produced in the adrenal cortex), and sex steroids (produced in the gonads or placenta). Within those two classes are five types defined according to the receptors they bind: glucocorticoids and mineralocorticoids (both corticosteroids), and androgens, oestrogens, and progestogens (sex steroids). Vitamin D has the chemical structure of a steroid hormone, is derived from cholesterol, and has similar effects to the corticosteroids and sex steroids, but is not part of one class.

Steroid hormones are generally carried in the blood, bound to specific carrier proteins. Further metabolism and catabolism occurs in the liver, in other peripheral tissues, and in target tissues. This guide will describe the regulation, synthesis, signalling, transport and metabolism of corticosteroids and sex steroids hormones.

Cholesterol is the precursor of steroid hormones. It travels through the blood on lipoproteins. Two types of lipoproteins carry cholesterol throughout the body: LDL (low-density lipoprotein) - called bad cholesterol as high levels raise the risk for heart disease and stroke - and HDL (high-density lipoprotein) - called good cholesterol as it absorbs cholesterol and carries it back to the liver.

Note: The term ‘steroid’ describes both hormones produced by the body and artificially produced medications that have a similar action.

Steroid Hormones

Progesterone

Progesterone is the only naturally produced progestogen in our body. It is made from pregnenolone, the ‘mother’ hormone. In women, progesterone prepares the lining of the uterus for implantation of the ovum (female reproductive cell). It is essential for the maintenance of pregnancy and for normal cycle regulation. Men also need progesterone (lower levels than women) to produce testosterone, and progesterone is involved in sperm development.

AlloP (Allopregnanolone) is made from progesterone and plays an important role in neurological functions. It exerts neuroprotective, antidepressant and anxiolytic effects via GABA receptors. Indeed, progesterone is typically regarded as the calming, anxiety-relieving hormone, and is important both in women and in men.

Symptoms of low progesterone in women include mood swings, migraines, PMS (premenstrual syndrome), fibroids, irregular/short cycle, painful/heavy periods, depression/anxiety, disrupted sleep, infertility/recurrent misacarriage, and accumulation of fat in the hips and thighs (along with oestrogen dominance). Symptoms of low progesterone in men include depression, irritability, low libido, erectile dysfunction, muscle loss, fatigue, and memory loss or trouble concentrating.

The CYP17A1 gene hydroxylates pregnenolone to androstenedione and progesterone to testosterone. Single Nucleotide Polymorphisms (SNPs) may upregulate this enzymatic activity, which can result in low progesterone, and higher cortisol and androgen levels. Additionally, stress and alcohol promote this pathway.

Whilst 5aR (5alpha-Reductase) is best known for converting testosterone into 5a-DHT and cortisol into 5a-THF, it also reduces progesterone to 5a-DHP using NADH as a cofactor. 5aR is coded by the SDR5A2 gene. A SNP on this gene slows its activity which may contribute to lower AlloP levels. It can also lead to higher cortisol levels, and adverse metabolic effects such as weight gain or insulin resistance. Lower 5aR activity is detrimental in the context of low levels of AlloP which have been associated with increased risk of anxiety and depression.

AKR1C4 is the gene that codes for 3alpha-hydroxysteroid dehydrogenase (3a-HSD), which converts 5a-DHP to AlloP with NADH as a cofactor. A SNP on AKR1C4 has been associated with a 66 to 80% decrease in the catalytic activity of the enzyme which may confer lower AlloP production and depression and anxiety.

In the context of PMDD (premenstrual dysphoric disorder), a cyclic mood disorder with paradoxical sensitivity to changes in AlloP levels, it has been hypothesised that stabilising AlloP levels could reduce symptoms of irritability, low mood, anxiety, food cravings and bloating.

SSRIs can directly enhance the conversion from 5a-DHP to AlloP, and have been shown to have a short onset of action (and at relatively low doses) which may help resolve irritability, affectivity lability and mood swings. Calcium, omega 3-fatty acids and evening primrose oil can also increase 3a-HSD's activity.

3a-HSD also plays an important role in deactivating other endogenous steroids (including 5a-DHT), as well as progestogens and prostaglandins. Thus, a SNP on AKR1C4 has been associated with increased mammographic density, and breast cancer risk with oestrogen and progestin therapy. 3a-HSD also helps to detoxify exogenous compounds containing a keto-group, including xenobiotics, environment pollutants and drugs.

GABA is the major inhibitory neurotransmitter in the brain where it acts on GABA-A receptors such as GABRA2. A SNP on GABRA2 is associated with a decreased GABRA2 receptor activity, and a reduced sensitivity to GABA and AlloP. This may increase the risk of anxiety. The medicinal herb valerian activates GABA receptors and L-theanine and rosemarinic acid (found in rosemary, lemon balm, sage, thyme and peppermint) can help maintain GABA levels by inhibiting its breakdown.

Cortisol

Cortisol is a glucocorticoid hormone which is mainly produced in the adrenal glands and is released with a diurnal cycle and in response to stress and low blood sugar. It raises blood sugar by gluconeogenesis (synthesis of new sugar) and by reducing insulin sensitivity. Cortisol also regulates and modulates inflammation (and inhibits the immune system), regulates hunger cravings, digestion, blood pressure, sleep/wake patterns and capacity to cope with stress.

5aR (5alpha-Reductase) converts cortisol into 5a-THF, which is inactive. If 5aR is slower, this can result in higher cortisol levels and less lipogenesis (fat synthesis). However, if 5aR is faster, this can lead to lower cortisol but more lipogenesis. An increased hepatic 5aR activity in insulin resistant patients may represent a compensatory response to clear hepatic cortisol in an attempt to preserve insulin sensitivity.

As the body perceives stress, adrenal glands make and release cortisol into the bloodstream. This causes an increase in heart rate and blood pressure while digestion and immunity are shut down. While having an efficient stress response is necessary, chronic production of cortisol can lead to complications such as insulin resistance and obesity.

An upregulated CYP17A1 gene (due to SNPs or stress) also sets the scene for a higher cortisol synthesis. This can potentially lead to a "pregnenolone steal", which is when high stress perception leads to an elevated use of pregnenolone for cortisol production, reducing the total amount of pregnenolone available for the production of other steroid hormones, such as progesterone.

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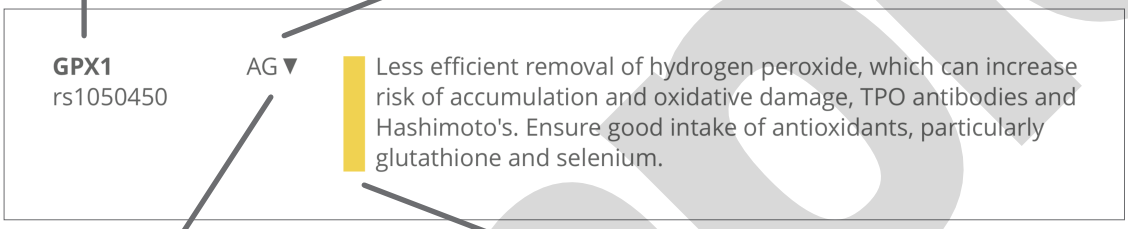
How to Read the Report

Genes

Results are listed in order of the gene short name. The 'rs' number is the reference sequence number that identifies a specific location on the genome. It is also known as a SNP (Single Nucleotide Polymorphism) pronounced 'snip', polymorphism or mutation.

Personalised Result

Your genotype result is shown as two letters (A,G,T or C) which represent the DNA bases present at that location.



Arrow Direction

The direction of the arrow indicates the potential effect of the SNP on gene expression, where applicable - it can increase or decrease activity, or neither.

▲ up-regulates or increases the activity and effect on the gene

▼ down-regulates or decreases the activity and effect on the gene

No arrow - no effect on the activity of the gene

Highlight Colour

The genotype result highlight indicates the potential effect of the SNP on gene function in a particular context.

RED the effect of the variant is negative

AMBER the effect of the variant is somewhat negative

GREEN no variation, or the effect of the variant is positive

Pathway Diagram Key

Cofactor Inhibitor

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ADRB1 Adrenoceptor Beta 1

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ADRB2 Beta-2-Adrenergic Receptor

Adrenergic-beta(2) receptor polymorphism and athletic performance. Vishnu Sarpeshkar and David J Bentley. J Hum Genet. 2010 Aug;55(8):479-85. doi: 10.1038/jhg.2010.42. Epub 2010 Apr 30. (https://pdfs.semanticscholar.org/735d/bd52384920347e78f9e188593b957887e2f6.pdf)

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AKR1C4 aldo-keto reductase family 1 member C4

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COMT Catechol-O-Methyltransferase

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CYP17A1 Cytochrome P450, Family 17, Subfamily A, Polypeptide 1

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CYP19A1 Cytochrome P450, Family 19, Subfamily A, Member 1

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