Lifecode GX ®
— Professional Genotype Analysis —

Oestrogen Balance Report

Oestrogen is one of the two major female steroidal sex hormones - the other being progesterone. The ovaries are the main source of oestrogen in females but it is also produced in smaller amounts by the adrenal glands and in fat tissue (more important post menopause), and also the placenta during pregnancy. Once produced, oestrogen moves through the blood and is active throughout the body in cells where oestrogen receptors (ERs) are present. ERs mediate the action of oestrogen and control gene expression.

There are two types of oestrogen receptors:
ER alpha - increases the action of the attached oestrogen
ER beta - decreases the action of the attached oestrogen

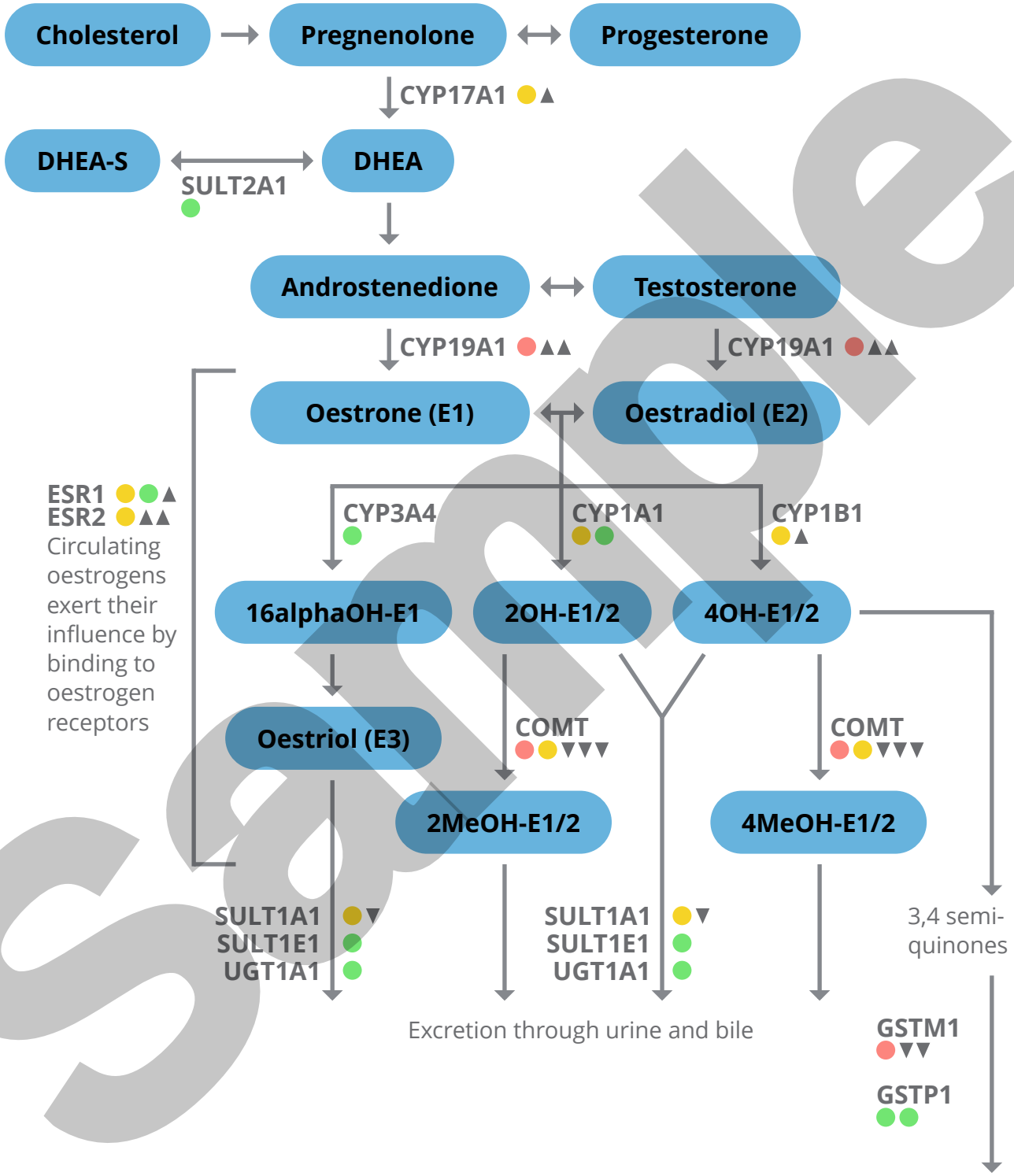
The main role of oestrogen in the body is to increase the growth and production of cells. It is responsible for the development and regulation of the female reproductive system and secondary sex characteristics - breasts, pubic hair etc. It is also involved in maintaining bone density, plays a role in blood clotting and affects skin, hair, mucous membranes and the pelvic muscles.

Oestrogen levels fluctuate throughout life, naturally increasing during puberty and pregnancy and falling after menopause. During the menstrual cycle, oestrogen levels peak during ovulation dropping off if pregnancy does not occur.

Men also produce and require oestrogen for the maturation of sperm and a healthy libido but at significantly lower levels.

There are three different types of oestrogen in the body:
Oestrone (E1) - predominant oestrogen produced after menopause
Oestradiol (E2) - predominant/most potent oestrogen in women of childbearing age
Oestriol (E3) - predominant oestrogen produced during pregnancy (also the weakest form)

Oestrogen Biosynthesis and Elimination



Detailed Results

COMT rs4633	TT ▼▼	Up to 4x lower COMT enzymatic activity leading to slow metabolism and inactivation of oestrogen via methylation. Poor methylation will further impede COMT activity due to low availability of SAMe. Review your MTHFR result below to see whether you might be a 'poor methylator'. A diet rich in B vitamins will help to improve methylation in general.
COMT	AG ▼	Reduced COMT activity leading to less efficient metabolism and inactivation of oestrogen via methylation. Poor methylation will further impede COMT activity due to low availability of SAMe. Review your MTHFR result to see whether you might be a 'poor methylator'. A diet rich in B vitamins will help to improve methylation in general.
CYP17A1	GA ▲	Up-regulated CYP17A1 enzyme activity, higher conversion of pregnenolone to androstenedione and testosterone, and elevated circulating oestrogens. Diet and lifestyle factors such a stress and excess adipose tissue increase CYP17A1 activity - ensure adequate physical activity and stress management techniques. Diindolylmethane (DIM)/cruciferous vegetables have been shown to decrease CYP17A1 activity.
CYP19A1	AA ▲▲	Increased conversion of androgens to oestrogen. Diet and lifestyle factors such as inflammation, excess adipose tissue, high insulin levels and stress will further increase CYP19A1 activity. Maintaining an ideal weight, balancing blood sugar, reducing inflammation and stress will help balance CYP19A1 activity. DIM, green tea and zinc have been shown to reduce CYP19A1 activity.
CYP1A1	TT	Normal (slow) CYP1A1 enzyme activity and normal (slow) hydroxylation of oestrogens to 2OH oestrogens. This is not beneficial if CYP1B1 and CYP3A4 pathways are up-regulated since it could lead to higher circulating 4OH oestrogens and 16aOH-E1 and lower 2OH oestrogens. Diindolylmethane (DIM), a compound derived from cruciferous vegetables, has been found to potently stimulate CYP1A1. Ensure phase II detoxification pathways are working optimally since increasing phase I enzymes can increase the production of free radicals. Antioxidants may be beneficial to neutralise free radicals.
CYP1A1	AA	Not associated with increased susceptibility to PCOS. Care should be taken to improve phase II metabolism.

A Guide to Oestrogen Balance

This guide contains detailed explanations of the lifecycle of oestrogen, from Biosynthesis (aromatisation and transformation) to Elimination (methylation and deactivation).

Biosynthesis and Genetics

Aromatisation

E1 and E2 are derived from the androgenic sex hormones testosterone and androstenedione via CYP19A1, a member of the cytochrome P450 superfamily of enzymes, which produces the enzyme aromatase - mainly found in the gonads, brain, adipose tissue, placenta, blood vessels, skin and bone, as well as in tissue of endometriosis, uterine fibroids, breast cancer, and endometrial cancer.

Variants on CYP19A1 can cause undesirable up-regulated conversion of androgens to oestrogens.

Hydroxylation

Once produced, oestrogen must be 'activated' via hydroxylation - the addition of an OH group (oxygen and hydrogen). Hydroxylated oestrogens, or catechol oestrogens, are released into circulation where they exert their influence by binding to ERs and can become potent, reactive and potentially harmful.

CYP1A1 is the most favourable of the hydroxylation pathways as it converts oestrogens into 2OH oestrogens which are neutral or even beneficial in the body.

Variants on CYP1A1 cause up-regulated enzyme activity which is desirable for oestrogen metabolism but can lead to high amounts of circulating pro-carcinogens if phase II detoxification pathways (methylation, sulphation, glucuronidation and glutathione conjugation) are not working optimally.

CYP1B1 converts oestrogens to 4OH oestrogens and can promote synthesis of the harmful molecules, 3,4 semi-quinones, which release free radicals, damage DNA and potentially initiate cancer.

Variants on CYP1B1 are associated with increased production of 4OH oestrogens and may also result in other circulating pro-carcinogens. It is particularly important for individuals with variants to ensure that the downstream phase II pathways are working optimally.

CYP3A4 converts E1 to 16alphaOH-E1, a strong form of oestrogen that binds to alpha ERs. CYP3A4 is also involved in the conversion of E2 to E3.

Variants on CYP3A4 result in up-regulation and care should again be taken to support downstream phase II detoxification pathways.

CYP17A1 hydroxylates pregnenolone and progesterone to androstenedione and testosterone, the initial step in oestrogen biosynthesis.

Variants cause up-regulated enzymatic activity and higher circulating oestrogens.

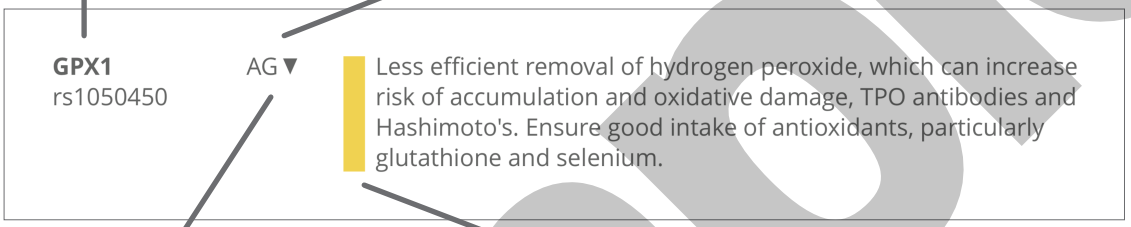
How to Read the Report

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

References

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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CYP1A1 Cytochrome P450, Family 1, Subfamily A, Polypeptide 1

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CYP1B1 Cytochrome P450, Family 1, Subfamily B, Polypeptide 1

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