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OverGenes

Genetics for people

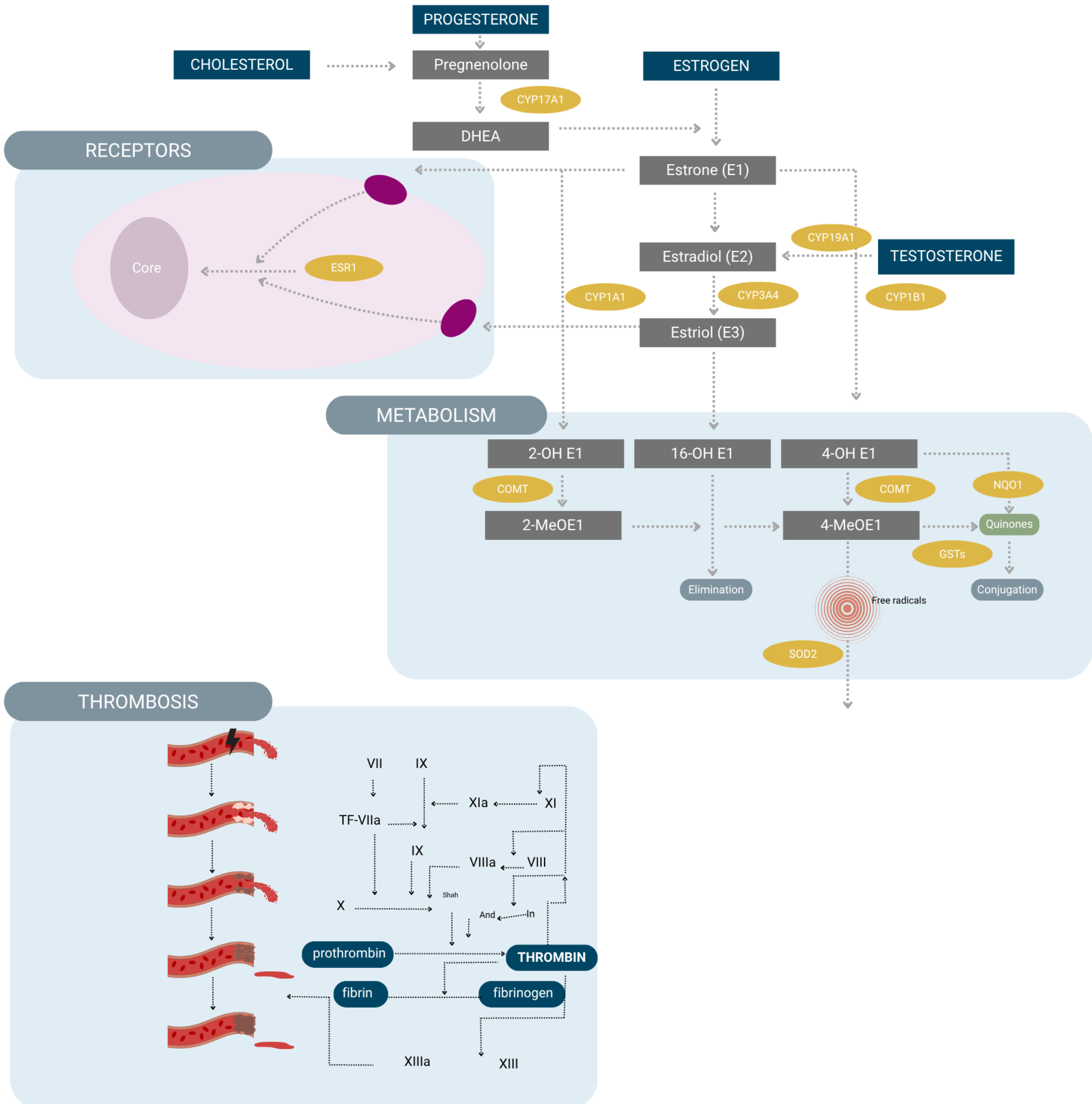
Genetic Testing Estrogens

My Estrogens

The genetic test MyEstrogen provides a comprehensive view of the role genetics plays in female hormonal balance. Through this analysis, the following are studied:

1. Estrogen metabolism: genes that influence the body's ability to transform and eliminate estrogens are identified, a key process to maintain adequate hormonal levels and reduce the accumulation of harmful metabolites.
2. Estrogen receptors: genes that mediate the action of these hormones in tissues are evaluated. Variations in receptor genes may affect the effectiveness of hormone replacement therapies and the body's response to estrogens.
3. Thrombosis risk: genes related to blood clotting are included, a fundamental aspect to consider in women who are evaluating hormonal treatments.

This study allows the personalization of medical care, guides decisions on hormone replacement therapy (HRT), and provides key information for the prevention of diseases associated with hormonal imbalance and cardiovascular risk.



GLOBAL RISK

ESTROGEN METABOLISM

Gene	Metabolizer	Clinical Impact
CYP1A1	NORMAL	Normal 2-OH formation
CYP1B1	SLOW	Reduced 4-OH formation
CYP3A4	NORMAL	Normal 16-OH formation

ESTROGEN RECEPTORS: **Unfavorable**

You present a polymorphism associated with resistance, which may result in lower effectiveness of hormone replacement therapy and a higher risk of adverse effects.

THROMBOSIS: **Limited Risk**

No risk variants studied in the development of thrombosis have been found.

ESTROGEN METABOLISM

Estrogen metabolism is a key process for maintaining hormonal balance and reducing the risk of harmful metabolite accumulation. It takes place in two main phases:

• **Phase I (hydroxylation):** At this stage, CYP450 family enzymes transform estrogens into intermediate metabolites.

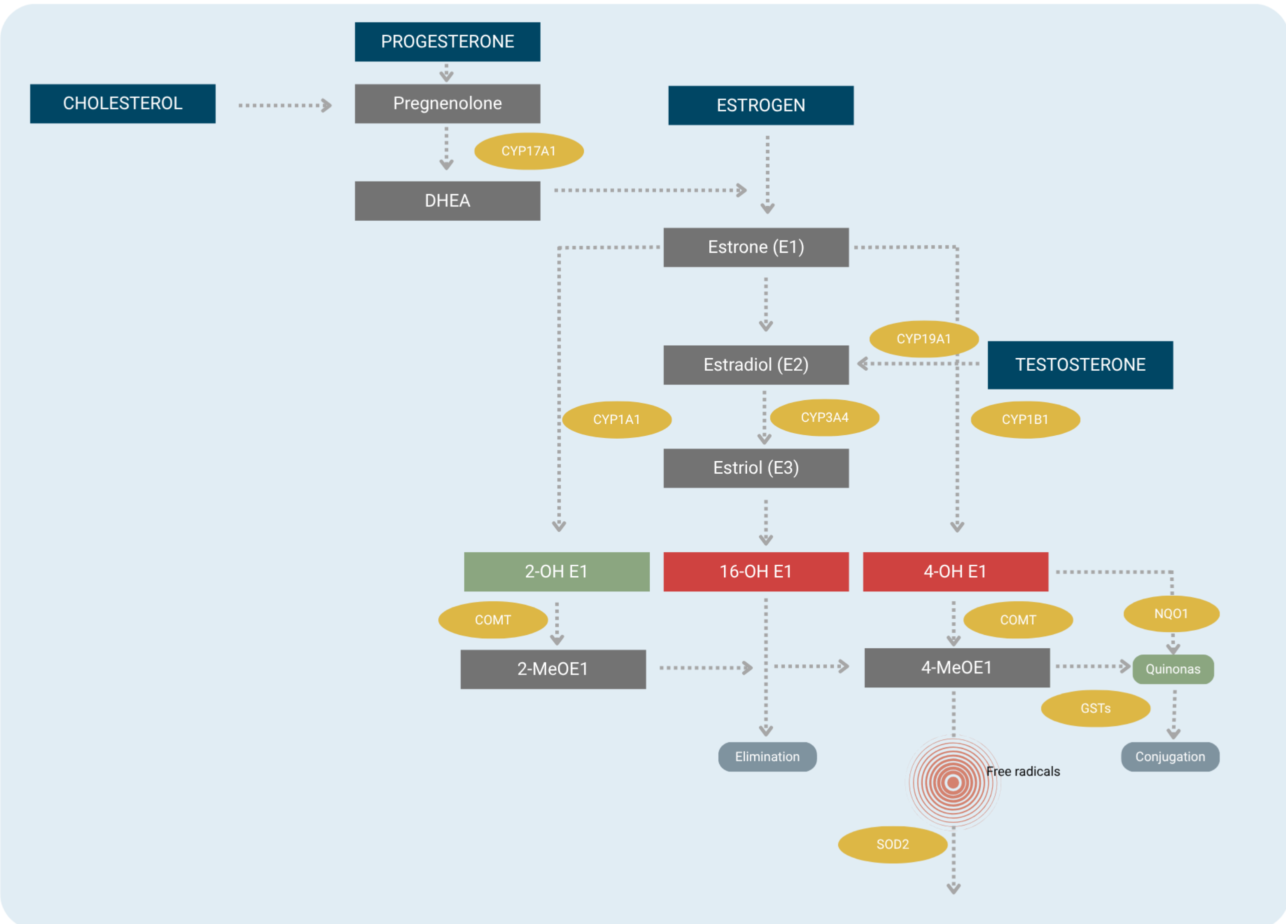
• **Phase II (conjugation and methylation):** Subsequently, the metabolites are conjugated to facilitate their excretion through urine and feces. An essential step is methylation, which inactivates the most reactive metabolites and reduces their potential to cause cellular damage.

Main estrogen metabolites:

• **2-OH-estrogens:** considered protective, with lower estrogenic activity and greater metabolic safety.

• **4-OH-estrogens:** potentially harmful, as they can form free radicals and damage DNA if not properly methylated.

• **16-OH-estrogens:** with stronger estrogenic activity and a proliferative effect that may be unfavorable in excess.



GENETIC RESULTS

The following table shows the variants detected in the patient. In the case of haplotypes, the type of metabolization is indicated based on the enzymatic activity of the allele:

Gene	Reference Haplotype	Patient Haplotype	Metabolizer
CYP17A1	TT	TT	–
CYP19A1	*1/*1	*1/*1	NORMAL
CYP1A1	*1/*1	*1/*2	NORMAL
CYP1B1	*1/*1	*2/*2	SLOW
CYP3A4	*1/*1	*1/*1	NORMAL
COMT	*1/*1	*1/*2	INTERMEDIATE
NQO1	Active/Active	Active/Active	NORMAL
SULT1A1	*1/*1	*2/*2	SLOW
GSTM1	*I/*I	*I/*I	NORMAL
GSTT1	*I/*I	*D/*D	SLOW
SOD2	*1/*1	*1/*1	NORMAL
MTHFR	*1/*1	*1/*2	INTERMEDIATE

RECOMMENDATIONS

Gene	Foods or Bioactive Compounds	
	Inhibitors	Inducers
CYP1A1	Black raspberry, Blueberries, Ellagic acid, Black soy, Black tea, Turmeric	Green tea, Black tea, Curcumin, Soy, Garlic, Fish oil, Rosemary, Astaxanthin
CYP1B1	Resveratrol, I3C, DIM, Sulforaphane, Licorice, Omega-3, NAC, Antioxidants (A, C, E, carotenoids, turmeric, green tea, lycopene, flavonoids), Alpha-lipoic acid, Curcumin, Selenium	Curcumin, Cruciferous vegetables
GSTM1 GSTT1	Cruciferous vegetables, Allium Citrus, Ghee, Sweet potato, Rosemary, Garlic, Curcumin, Fish oil, Resveratrol Black soy, Ellagic acid, Green tea, Rooibos, Honeybush	Apiaceous vegetables Quercetin Genistein
CYP3A4	Curcumin	Resveratrol, Myricetin, Soybean, Kale, Grapefruit, Garden cress
SULT1A1		**Avoid** caffeine, cocoa, tea, high levels of vitamin A
COMT		**Avoid** green tea Resveratrol, Vitamin B6 Stress management

ESTROGEN RECEPTORS -

Hormone Replacement Therapy

In hormonal processes related to female health, estrogen and progesterone receptors play a key role. These proteins, upon binding to their specific hormones, trigger cellular responses such as protein synthesis and regulation of vital functions.

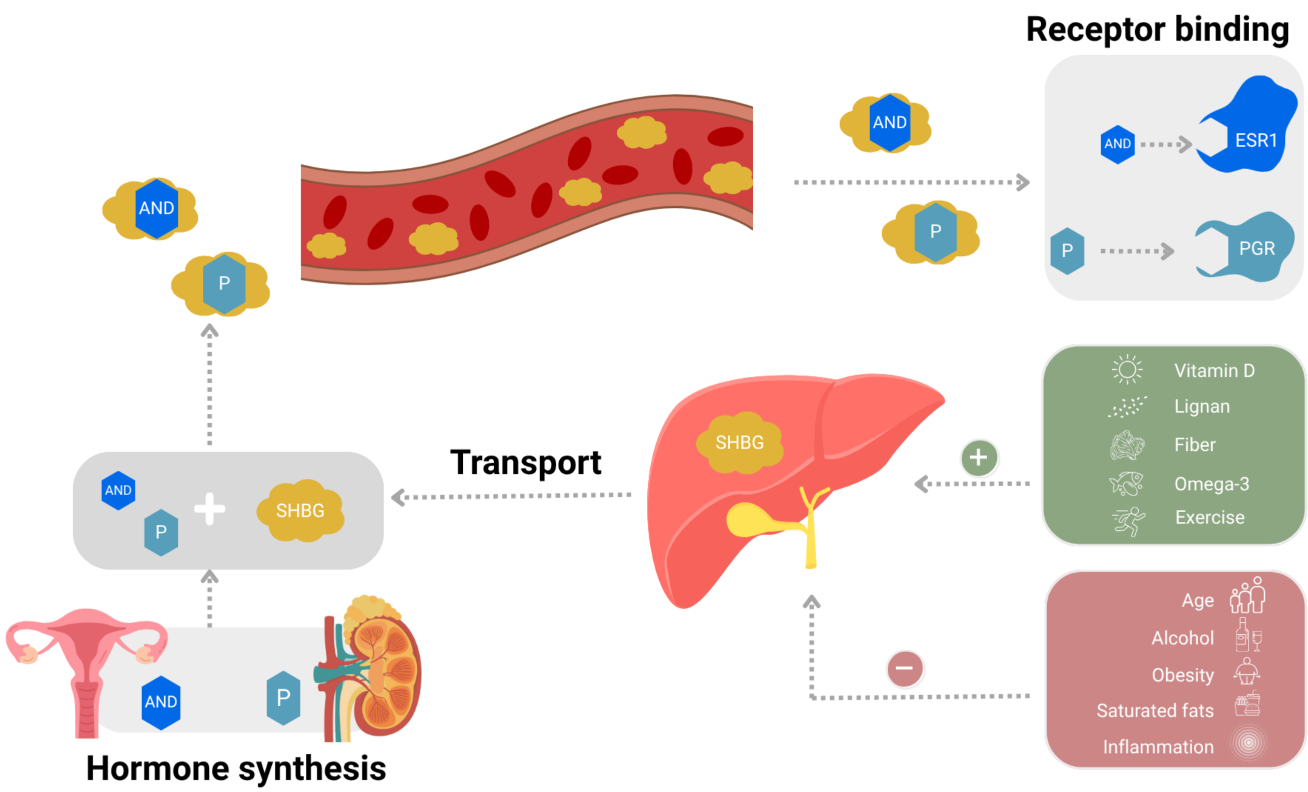
Estrogen Receptors (ER):

• **ESR1:** its activation promotes a proliferative effect, supporting cell growth. Genetic variants capable of modifying the receptor structure have been identified. These alterations may change the affinity for estrogens and, consequently, modulate the effectiveness of hormone replacement therapy.

• **ESR2:** exerts a modulatory effect, balancing the estrogenic response. No relevant functional polymorphisms have been described.

Progesterone Receptor (PGR):

It also presents genetic variants that can influence its function.
Although they have not been directly associated with an increased risk of breast cancer, a relationship has been observed with a higher risk of uterine pathologies.



GENETIC RESULTS

The following table shows the variants detected in the patient:

Gene	Marker	Reference Genotype	Patient Genotype
ESR1	rs2234693	TT	TC
PGR	rs1042838	CC	CC

You present a polymorphism associated with resistance, which may translate into lower effectiveness of hormone replacement therapy and a higher risk of adverse effects.

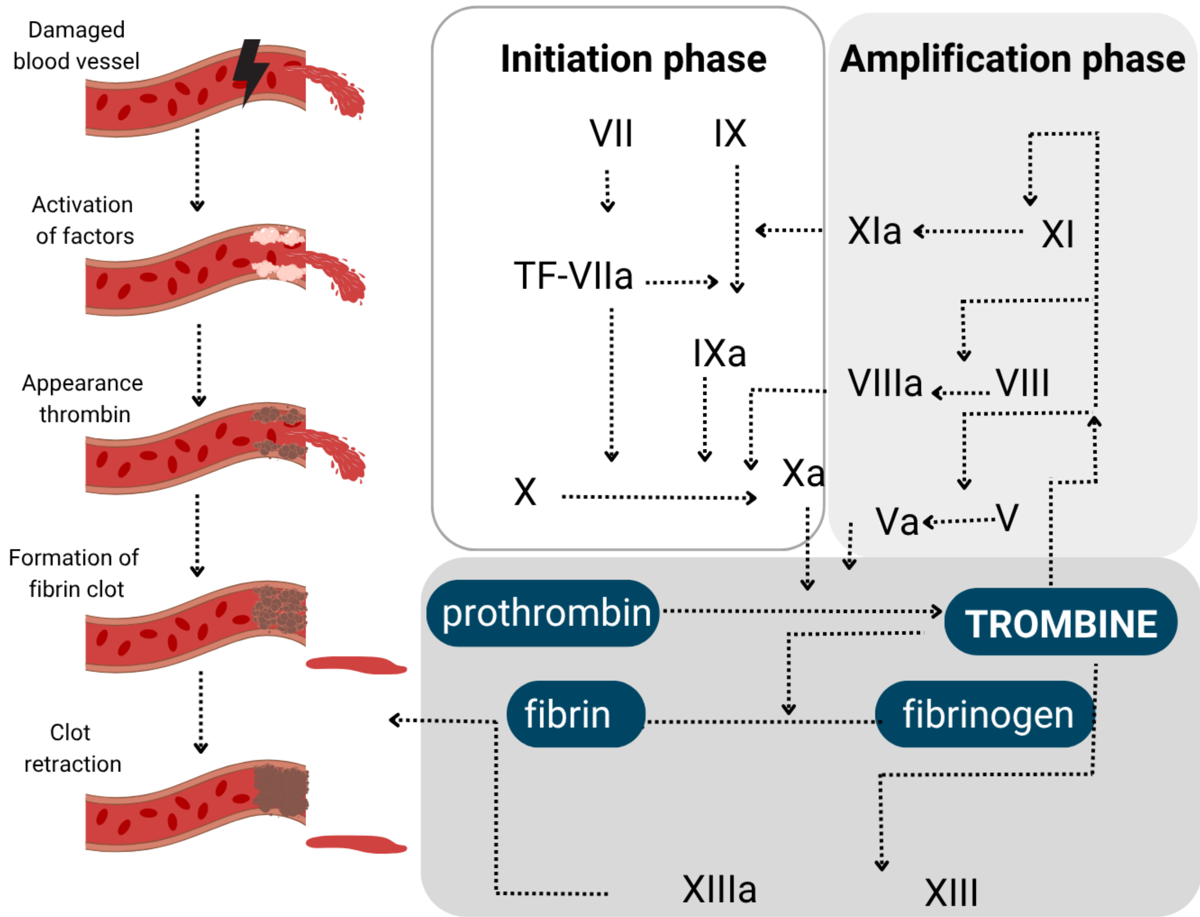
RECOMMENDATIONS

Gene	Action	Foods or Bioactive Compounds
ESR1	**Reduce** the increase of alpha receptors (proliferative)	**Reduce** consumption of pro-inflammatory foods such as alcohol, processed meats and cold cuts, wheat, white sugar, sweeteners, and additives. **Avoid** xenoestrogens and/or endocrine disruptors: BPA-bisphenol, acrolein (grilled, barbecued, or fried foods), mercury amalgams, benzenes and ethylbenzenes, epoxides, herbicides and pesticides, HPA, quinones, tobacco smoke, etc. **Consume** sauerkraut and cabbage, phytoestrogens, naringenin, Reishi, indole-3-carbinol, and diindolylmethane.
PGR	**Increase** the modulatory action of beta receptors (antiproliferative)	**Anti-inflammatory diet:** Leafy greens and vegetables, berries, legumes, fish, nuts, seeds, extra virgin olive oil, spices, etc. **Consume** licorice, kudzu, rhubarb or chasteberry, lignans, or sage.

THROMBOSIS

Limited Risk

Deep vein thrombosis (DVT) is a condition that occurs when a blood clot forms in a deep vein. These clots typically form in the lower legs, thighs, or pelvis, although they can also appear in other parts of the body, such as the upper limbs.



GENETIC RESULTS

Below is the impact of your genetics on the analyzed genes.

Gene	Impact
MPL	●
PROS1	●
SER-PINC1	●
ACVRL1	●
ENG	●

● No risk alleles ● One risk allele ● At least two risk alleles

Additionally, the classification of risk derived from polygenic inheritance is shown:

OTHER GENES ANALYZED	POLYGENIC RISK
F5, F2, ABO, TSPAN15, FGG, F11, CATSPER2, C4BPA, PROCR, SERPINA1, CSRNP1, CYB5R3, APOH, VWF, ZFPM2, FADS1, ORC3, ACAD10, FCER1G, F9, TC2N, ILRUN, PPP1R3B, SERPINE2, XXYLT1, ARHGAP24, QSER1, HSD3B7, JAZF1, COPZ1, CPS1, MPHOSPH9, TENT5C, LINC00880, NEK4, TOMM20L, CELSR2, AK5, DCST2, RSPH6A, CARMIL1, LINC02323, TAOK1, LINC00924, LINC02652, MLLT10, MS4A4A, ARHGEF28, MIR497HG, RORA, ZBTB16, ERAP2, PLCE1, CALCRL, FAM168A, RAB4B, PLEK, TRIM58, STXBP5, OSMR, KNG1, HCG9, SMG6, MAPT, F10, SOX6, SCARA5, PROC, HSPA4, LINC03125, PLCG2, GP6, ABCA5, SLC44A2, GRK5, ARL13B	●●●

●●● Normal ●●● Moderate ●●● High

RECOMMENDATIONS

Nutrient	Main Foods
Omega-3 (EPA, DHA, ALA)	Fatty fish (salmon, sardine, mackerel), walnuts, flaxseed, and chia seeds
Vitamin E	Extra virgin olive oil, avocado, almonds, hazelnuts, sunflower seeds
Polyphenols and flavonoids	Berries, black grapes, pomegranate, dark chocolate (>70 %), green tea
Vitamin C	Citrus fruits, kiwi, red bell pepper, broccoli
Natural nitrates	Beetroot, spinach, arugula, celery
Soluble fiber	Oats, legumes, apple, citrus fruits
Spices	Turmeric, ginger, garlic, onion
Hydration	Water, green tea
Nuts	Pistachios, hazelnuts, almonds
Soy and isoflavones	Soy and soy products
Vitamin K	Spinach, broccoli, kale, romaine lettuce (consume in moderation depending on treatment)

APPENDIX I: DETAILS OF THE ANALYZED GENES

CYP17A1 rs2486758	
This gene encodes a member of the cytochrome P450 enzyme family that catalyzes the final steps in estrogen biosynthesis. Mutations in this gene may lead to increased or decreased aromatase activity, the enzyme responsible for converting androgens to estrogens. The TT genotype is associated with **normal enzyme activity**.	Patient Genotype: **TT**

CYP19A1	
This gene encodes a member of the cytochrome P450 enzyme family that catalyzes the final steps in estrogen biosynthesis. Mutations in this gene may lead to increased or decreased aromatase activity, the enzyme responsible for converting androgens to estrogens. According to his haplotype the patient is a CYP19A1 **normal metaboliser**.	Patient Haplotype: ***1/*1**

CYP1A1	
This gene encodes a member of the cytochrome P450 enzyme family and its expression is induced by polycyclic aromatic hydrocarbons, present in toxic substances such as tobacco smoke, which have a procarcinogenic effect. It is also involved in the oxidative metabolism of estrogens, playing an important role in the development of breast and prostate cancer. According to his haplotype the patient is a CYP1A1 **normal metaboliser**.	Patient Haplotype: ***1/*2**

CYP1B1	
This gene encodes a member of the cytochrome P450 enzyme family that metabolizes procarcinogens such as polycyclic aromatic hydrocarbons. It is also involved in the oxidative metabolism of estrogens, playing an important role in the development of breast and prostate cancer. According to his haplotype the patient is a CYP1B1 **slow metaboliser**.	Patient Haplotype: ***2/*2**

CYP3A4	
This gene encodes a member of the cytochrome P450 enzyme family and its expression is induced by glucocorticoids and certain drugs. It participates in the metabolism of commonly used drugs such as paracetamol, codeine, and diazepam, as well as steroids and carcinogens. According to his haplotype the patient is a CYP3A4 **normal metaboliser**.	Patient Haplotype: ***1/*1**
COMT	
Catechol-O-methyltransferase is an enzyme encoded by the COMT gene that catalyzes the transfer of a methyl group from S-adenosylmethionine to catecholamines, allowing regulation of certain hormone levels. Accumulation of metabolites from the estrogen pathway increases the risk of developing breast cancer. According to his haplotype the patient is a COMT **intermediate metaboliser**.	Patient Haplotype: ***1/*2**
NQO1	
This gene belongs to the NAD(P)H quinone oxidoreductase family and encodes a cytoplasmic reductase. This FAD-binding protein forms homodimers and reduces quinones to hydroquinones. The enzymatic activity of this protein prevents one-electron reduction of quinones that leads to the production of radical species, thus contributing to the detoxification of highly mutagenic and carcinogenic quinones from tobacco, diet, and estrogen metabolism. According to his haplotype the patient is a NQO1 **normal metaboliser**.	Patient Haplotype: **Active/Active**

GSTM1	
This gene encodes a glutathione S-transferase involved in the detoxification of electrophilic compounds, including carcinogens, therapeutic drugs, environmental toxins, and products of oxidative stress, via conjugation with glutathione. These genetic variations can modify an individual's susceptibility to carcinogens and toxins, as well as affect the toxicity and efficacy of certain drugs. According to his haplotype the patient is a GSTM1 **normal metaboliser**.	Patient Haplotype: ***I/*I**

GSTT1	
The protein encoded by this gene, glutathione S-transferase theta 1 (GSTT1), is a member of a superfamily of proteins that catalyze the conjugation of reduced glutathione with diverse electrophilic and hydrophobic compounds. According to his haplotype the patient is a GSTT1 **slow metaboliser**.	Patient Haplotype: ***D/*D**

SOD2	
This gene encodes an essential enzyme in the folate cycle. Its main function is to convert 5,10-methylenetetrahydrofolate into 5-methyltetrahydrofolate, the active form of folate that participates in the remethylation of homocysteine to methionine. According to his haplotype the patient is a SOD2 **normal metaboliser**.	Patient Haplotype: ***1/*1**

MTHFR	
This gene encodes a protein that binds superoxide by-products from oxidative phosphorylation and converts them into hydrogen peroxide and diatomic oxygen, eliminating free radicals generated from various biological processes. According to his haplotype the patient is a MTHFR **intermediate metaboliser**.	Patient Haplotype: ***1/*2**

ESR1 rs2234693	
Gene encoding one of the two main types of estrogen receptor proteins. These proteins bind to the estrogen hormone and receive its signals. They are found inside cells of female reproductive tissue, breast tissue, and many other tissue types, as well as in some cancer cells. Once activated by estrogens, estrogen receptors control the activity of specific genes important for cell proliferation and metabolism, sexual development, pregnancy, and other reproductive functions. The patient's ESR1 genotype is associated with **altered** receptor structure and function.	Patient Genotype: **TC**

PGR rs1042838	
This gene encodes a member of the steroid receptor superfamily. The encoded protein mediates the physiological effects of progesterone, which plays a central role in reproductive events associated with the establishment and maintenance of pregnancy. The detected genotype for the PGR gene is associated with **normal activity**, indicating an appropriate response to progesterone.	Patient Genotype: **CC**

ANNEX II: RECOMMENDED NUTRIENTS and EFSA EVALUATION

ESTROGEN METABOLISM

Nutrient	Claim	Condition of use
	AUTHORIZED (Reg. (EU) 432/2012)	
Vitamin B6	Contributes to the regulation of hormonal activity	≥15 % NRV (≥0.21 mg/serving). Art.13(1)
Zinc	Contributes to normal fertility and reproduction	≥15 % NRV (≥1.5 mg/serving). Art.13(1)
Selenium	Contributes to normal spermatogenesis	≥15 % NRV (≥8.25 μg/serving). Art.13(1)
Folate (B9)	Contributes to maternal tissue growth during pregnancy	≥15 % NRV (≥30 μg/serving). Art.13(1)
	NOT AUTHORIZED BY EFSA	
Soy / Red Clover Isoflavones	Claims for relief of menopausal symptoms rejected	—
Flaxseed Lignans	Claims for hormonal balance rejected	—
Black Cohosh	Not approved; liver safety alerts	—
Resveratrol / Polyphenols (grape, green tea)	Claims for hormonal balance or menopause rejected	—
Turmeric / Curcumin	Claims for hormonal regulation rejected	—
	NOVEL FOODS	
Soy Isoflavones	No approved claims for estrogens or menopause	—
Red Clover	No approved claims for estrogens or menopause	—
Flaxseed Lignans	No approved claims	—
Resveratrol	No claims on estrogen metabolism or menopause	—
Adaptogenic Extracts (maca, ashwagandha)	No approved claims in the EU	—
CBD / Cannabinoids	Under EFSA evaluation, no approved claims	—

THROMBOSIS

Nutrient	Claim	Condition of use
AUTHORIZED (Reg. (EU) 432/2012)		
Calcium	Contributes to normal blood coagulation	≥15 % NRV (120 mg per serving). Art.13(1)
EVALUATED		
Tomato Soluble Concentrate	Evaluated for platelet function and coagulation time	—
NOT AUTHORIZED BY EFSA		
Omega-3 (EPA/DHA)	Promoted for circulation and thrombosis reduction	—
Vitamin E	Promoted as anticoagulant and vascular protector	—
Polyphenols (e.g., resveratrol)	Promoted for cardiovascular prevention	—

TECHNOLOGY

DNA Microarray technology consists of a solid surface with microscopic reactions (micro-reactions) or DNA chips, on which molecular probes are fixed to detect the presence of target DNA molecules. Probe-target hybridization is usually detected and quantified by measuring, in the samples, the intensity of a specific fluorescence provided by the molecular probe. This technology allows the detection of thousands of specific DNA fragments present in a DNA sample. Moreover, the specificity for recognizing DNA sequences is very high, as single nucleotide changes can be detected (single-base resolution) using short oligonucleotide probes (20–25 nucleotides). As a result, DNA Microarray technology has also evolved to be applied as a DNA sequencing technique to genotype several hundred thousand single nucleotide variants (SNVs) in target genes located throughout the genome (Whole Genome DNA Microarray).

QUALITY

The analysis laboratory follows standard and effective procedures to prevent technical and operational issues. However, results may be affected due to problems with sample collection (contamination) and labeling (identification), delays in sample reception at the laboratory (integrity), among other issues. This could lead to invalid test results. In such cases, the patient would be asked to repeat the entire process for the test.
As with all laboratory tests, there is a small possibility that the laboratory may report inaccurate information. If there is suspicion of an error regarding the detected genotype, a verification analysis could be requested.

GLOSSARY

• **DNA:** abbreviation for deoxyribonucleic acid. Molecule present in our cells that contains the genetic information necessary for the development and proper functioning of living organisms.

• **Allele:** each of the alternative forms of a gene, which may differ in sequence.

• **Androgens:** Steroid hormones that stimulate the development and maintenance, especially of male characteristics in the human body, such as facial hair and muscle development.

• **Cell:** basic structural and functional unit of life.

• **Estrogens:** Group of sex hormones responsible for developing and maintaining female secondary sexual characteristics, as well as regulating the menstrual cycle.

• **Gene:** DNA segment that represents the unit of hereditary information.

• **Haplotype:** Set of alleles at a specific group of loci on a chromosome that tend to be inherited together.

• **Heterozygous:** when the two alleles of the same gene are different.

• **Homozygous:** when the two alleles of the same gene are identical.

• **Hormone:** Chemical messenger in the body that regulates various physiological functions such as growth, development, metabolism, and reproduction.

• **Progesterone:** Female sex hormone that plays a crucial role in the menstrual cycle and the maintenance of pregnancy.

• **Testosterone:** Primary male sex hormone, responsible for the development of primary and secondary sexual characteristics in men.

Genetics for people

Contact:

Scientific Park
Valencia University

St, Agustín Escardino Benlloch, 9
Paterna, Valencia

(+34)96 321 77 58
info@overgenes.com

www.overgenes.com