GENOMICA
Next Generation Genetics

Genetic profiling of biological processes relevant to preconception and pregnancy health



An integrated assessment of genetic predispositions throughout the reproductive journey, from preconception to breastfeeding.

- Preconception
- Pregnancy
- Prevention
- Nutrition

PREGNANCYPROFILE

PREGNANCYPROFILE

PREGNANCY:A COMPLEX BIOLOGICAL SYSTEM

From preconception through breastfeeding, the maternal body undergoes profound metabolic, cardiovascular, haematological, endocrine and immune adaptations. Embryo implantation, placental development and fetal growth require the coordination of numerous processes: nutrient metabolism, DNA synthesis and repair, epigenetic regulation of gene expression, plasma volume expansion, uterine artery remodelling, iron homeostasis, lipid metabolism, and the balance between inflammation and maternal-fetal immune tolerance.

These systems are interconnected and share some of the same mechanisms. Their overall balance depends on a coordinated response to metabolic demands that increase throughout pregnancy.

Pregnancy outcomes therefore reflect the interaction of multiple factors and cannot be attributed to a single determinant. Age, pre-existing medical conditions, diet, lifestyle, environmental exposures, and personal and family medical history all contribute to the individual context, alongside **genetic factors**.

An integrated assessment of maternal health

Medical and reproductive history

Reproductive history, family history, pre-existing conditions and recognised risk factors.

Maternal health

Blood pressure, metabolic status, organ function and clinical course.

Nutrition and lifestyle

Diet quality, nutrient intake, physical activity, sleep and daily habits.

Medication and exposures

Medication, supplements, smoking, alcohol, and occupational or environmental exposures.

Genetic profile

Stable genetic information, interpreted in the individual's clinical and personal context.

Monitoring

Clinical, obstetric and laboratory assessments as indicated.

PREGNANCYPROFILE

THE TEST

PREGNANCYPROFILE is a genetic test that analyses **24 selected variants** in **17 genes** involved in metabolic, nutritional, vascular and immune processes relevant to preconception health, pregnancy and breastfeeding.

The resulting **profile** provides a structured overview of selected **genetic predispositions** in the person tested, to be considered alongside medical history, diet, lifestyle and clinical findings. It offers information to support gynaecologists, other healthcare professionals and women throughout the reproductive journey.

24	17	5
VARIANTS	GENES	FUNCTIONAL AREAS

The areas covered include:

1. **One-carbon metabolism, folate, choline and transsulfuration**
2. **Vascular regulation, placentation, blood pressure and fetal growth**
3. **Iron homeostasis and trace elements**
4. **Lipid metabolism, polyunsaturated fatty acids and responses to xenobiotics**
5. **Immune and inflammatory balance**

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PURPOSE OF THE TEST

- describe the potential contribution of selected variants to folate and choline metabolism, transsulfuration, vascular and placental function, iron homeostasis, lipid metabolism and immune regulation;
- highlight potential converging effects among variants involved in the same biological pathway;
- support consideration of further clinical or laboratory investigations, where appropriate;
- provide general guidance on diet and lifestyle.

THE REPRODUCTIVE JOURNEY

WHEN TO CONSIDER TESTING

Before conception

To review diet, habits, medication and supplements; assess personal and family medical history; identify modifiable risk factors; and plan clinically indicated investigations.

During pregnancy

As complementary information on maternal metabolic, vascular and haematological adaptations, alongside the assessments included in the care pathway.

During breastfeeding

For aspects of the test concerning nutrients and metabolic pathways that are also relevant to milk production and newborn development.

PREGNANCYPROFILE

THE GENETIC PANEL

The **five functional areas** make the report easier to navigate. This grouping is for clarity: many genes participate in more than one process, and the biological pathways covered are closely interconnected.

Biological area	Genes	Variants
1 **One-carbon metabolism, folate and choline**	*CBS, MTHFD1, MTHFR, BHMT*	**9**
2 **Vascular regulation and placentation**	*CYP11B2, LRP8, CDKN2B-AS1 (ANRIL)*	**4**
3 **Iron homeostasis and trace elements**	*HFE, TMPRSS6*	**3**
4 **Lipids, fatty acids and responses to xenobiotics**	*ADIPOQ, GSTP1, FADS2, FADS1*	**4**
5 **Immune and inflammatory balance**	*TNF, IL1B, IL17F, IL17A*	**4**
TOTAL	**17 genes**	**24**

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AREA 1

ONE-CARBON METABOLISM, FOLATE, CHOLINE AND TRANSSULFURATION

One-carbon metabolism links nucleotide synthesis, methylation, homocysteine remethylation, transsulfuration and choline metabolism. This network of reactions is particularly relevant around conception: the neural tube closes by the fourth week after conception, often before pregnancy is recognised, during a period of intense cell proliferation and embryonic epigenetic reprogramming.

The function of these pathways depends on the interaction between genetic factors, nutritional status, absorption, medication and clinical conditions.

Genes	Biological role
CBS ***MTHFD1*** ***MTHFR***	**Transsulfuration, folate metabolism and the availability of one-carbon units.** **CBS** participates in transsulfuration, the pathway that uses homocysteine to produce cysteine and, subsequently, glutathione. **MTHFD1** and **MTHFR** are involved in folate metabolism and the availability of the active forms required for methylation.
BHMT	Contributes to the conversion of homocysteine back to methionine using betaine, which is also derived from choline. It thus links choline intake to the efficiency of methylation reactions.

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AREA 2

VASCULAR REGULATION AND PLACENTATION

The maternal cardiovascular system undergoes important adaptations from early pregnancy. Plasma volume and cardiac output increase, while peripheral vascular resistance decreases. The renin-angiotensin-aldosterone system adapts to support the sodium and water retention needed to expand circulating volume. During the first trimester and the beginning of the second, extravillous trophoblast invades the decidua and remodels the uterine spiral arteries into dilated, low-resistance vessels capable of maintaining a high, steady blood flow to the placenta.

Incomplete remodelling may reduce placental perfusion and promote hypoxia and oxidative stress. The resulting release of antiangiogenic factors and inflammatory mediators may damage the maternal endothelium. These processes play a central role in the pathogenesis of **pre-eclampsia** and, through somewhat different mechanisms, **fetal growth restriction**.

PREGNANCYPROFILE analyses variants in genes involved in blood pressure regulation and cell signalling, together with regions associated with complex vascular traits.

Genes	Biological role
CYP11B2	Participates in aldosterone synthesis and blood pressure regulation. Its regulatory variants have been studied for their potential influence on gene expression, aldosterone production, the aldosterone-to-renin ratio and susceptibility to hypertension.
LRP8	In placental cells, participates in lipid transport and signalling pathways involved in the placental response to stress. These processes may influence nutrient availability to the fetus, fetal growth and birth weight.
CDKN2B-AS1 (ANRIL)	A regulatory locus at 9p21.3 with widely replicated associations with vascular and cardiometabolic traits. It has also been investigated in relation to pre-eclampsia, a condition involving alterations in endothelial function, immune regulation and trophoblast invasion.

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AREA 3

IRON HOMEOSTASIS AND TRACE ELEMENTS

Iron requirements increase during pregnancy to support maternal red blood cell production, placental development and fetal growth, as well as the establishment of the newborn's iron stores for the first months of life.

Maternal red blood cell production

Placental development

Fetal growth

Newborn's iron stores for the first months of life

Iron status depends on diet, absorption, inflammation, losses, supplementation and genetic variability. The panel analyses selected variants in **HFE** and **TMPRSS6**, which have different implications for interpretation.

HFE

Contributes to the regulation of iron absorption. The test analyses the **p.His63Asp (H63D)** and **p.Cys282Tyr (C282Y)** variants. Certain combinations, particularly C282Y homozygosity, may have specific clinical relevance to a predisposition to HFE-related hereditary haemochromatosis. Penetrance is incomplete: genetic predisposition does not mean that iron overload is present.

TMPRSS6

Participates in the regulation of hepcidin, the hormone that controls iron absorption and distribution. The variant analysed is associated with quantitative differences in red blood cell indices and iron metabolism parameters.

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AREA 4

LIPID METABOLISM, POLYUNSATURATED FATTY ACIDS AND RESPONSES TO XENOBIOTICS

This area covers genes involved in maternal metabolic adaptation mediated by adipose tissue, the availability of long-chain polyunsaturated fatty acids for fetal development, and cellular responses to certain xenobiotics: substances foreign to the body that originate from the environment or from specific exposures.

Genes	Biological role
ADIPOQ	Encodes adiponectin, which helps modulate maternal insulin sensitivity and the signals regulating placental nutrient transport. Variations in its circulating concentrations have been studied in relation to maternal obesity, gestational diabetes and fetal growth.
FADS2 ***FADS1***	Encode enzymes involved in converting essential omega-3 and omega-6 precursors into long-chain fatty acids, including DHA and EPA. Variants in the FADS cluster are associated with average differences in circulating fatty acid profiles.
GSTP1	Encodes an enzyme that uses glutathione to transform certain compounds, including xenobiotics, contributing to cellular conjugation processes and responses to specific exposures.

Adipose tissue
Maternal metabolic adaptation

Omega-3 and omega-6
long-chain fatty acids for fetal development

Xenobiotics
Cellular response to substances foreign to the body

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AREA 5

IMMUNE AND INFLAMMATORY BALANCE

During pregnancy, the maternal body must maintain effective defences against infection while tolerating the trophoblast, an embryonic tissue that also expresses paternal antigens. This balance changes throughout gestation. Implantation and trophoblast invasion require a physiological inflammatory response that is locally regulated and limited in time. This is followed by a prolonged phase favouring tolerance, which is necessary for fetal growth; near term, renewed inflammatory activity contributes to the onset of labour.

TNF, **IL1B**, **IL17F** and **IL17A** encode cytokines, the messengers that regulate immune and inflammatory responses. Their activity forms part of complex networks that vary according to tissue and stage of pregnancy.

Genes	Biological role
TNF	Encodes a proinflammatory cytokine. Physiological concentrations support normal immune function and may contribute to implantation and placentation. Excessive, persistent or inadequately regulated production may promote endothelial dysfunction, altered trophoblast invasion and imbalances in maternal-fetal tolerance. Elevated concentrations have been observed in several obstetric complications, including recurrent pregnancy loss, pre-eclampsia and preterm birth.
IL1B	Encodes interleukin-1 beta, a proinflammatory cytokine. Appropriate, time-regulated production may contribute to physiological implantation, trophoblast invasion and placentation. An excessive or persistent response may promote a proinflammatory environment in the endometrium and placenta, while an insufficient response could interfere with signals required in early pregnancy.
IL17F ***IL17A***	Participate in the IL-17 pathway and modulation of the immune response. In reproduction, Th17/IL-17A activity must remain balanced with regulatory T-cell activity and other mechanisms of maternal-fetal tolerance. An excessive or persistent Th17 response has been observed in certain obstetric conditions, including recurrent pregnancy loss and pre-eclampsia.

PREGNANCYPROFILE

A CLEAR REPORT THAT IS EASY TO NAVIGATE

For each variant analysed, the report provides the **genotype**, meaning the combination of alleles observed, and assigns it to a descriptive category. These categories summarise the direction of the association reported in the literature, helping healthcare professionals interpret the results and explain them to the person tested.

Descriptive category	Interpretation
● **Greater attention**	A genotype with two alleles associated with an **unfavourable effect,** calling for closer attention to relevant modifiable factors.
● **Intermediate profile**	A genotype associated with an **intermediate effect**, generally less pronounced and often corresponding to a heterozygous genotype.
○ **Expected**	A genotype without the allele associated with an unfavourable effect, with function or susceptibility considered typical for the variant examined.
● **More favourable profile**	A genotype with two alleles associated with a **favourable** or **protective effect** in the selected studies.
● **Intermediate favourable profile**	A genotype with one allele associated with a favourable effect of intermediate degree.
○ **Reference profile**	A genotype without the favourable allele, corresponding to the population baseline risk and not indicating increased risk.

The presence of several genotypes associated with effects in the same direction within a given area may draw attention to aspects that warrant further consideration, the quality of dietary intake or relevant modifiable factors.

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WHAT THE REPORT CONTAINS

- identification of the variants analysed and the genotypes detected;
- functional annotation and a summary of selected associations for each marker;
- results organised by biological area to support an integrated interpretation of the profile;
- general guidance on diet, lifestyle and topics to discuss with healthcare professionals;
- a description of the analytical and interpretative limitations.

WHAT THE TEST INCLUDES

Personalised report

Provides the genotype detected for each of the 24 variants and an interpretation of the results by biological area, according to the **PREGNANCYPROFILE** model.

Technical report

Describes the purpose, biological basis, methodology, interpretation criteria and limitations of the test. For each area, it details gene functions, the variants analysed and the meaning of possible genotypes, with key scientific references.

Genetic counselling

Personalised genetic counselling accompanies the report and explains what the profile means for the individual.

Interpretative support

The laboratory assists the requesting healthcare professional with methodological and interpretative questions about the results.

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FROM SAMPLE TO PERSONALISED REPORT

The analytical workflow comprises **six** stages:

1

DNA extraction

Isolation of genomic DNA from a buccal swab or peripheral blood sample.

2

Target region preparation

Targeted amplification or enrichment of regions containing the variants analysed, using a PCR-based protocol.

3

Sequencing

Analysis using next-generation sequencing (NGS) to determine the genotypes.

4

Bioinformatics analysis and genotyping

Processing of sequencing data using dedicated bioinformatics procedures to identify alleles and assign the genotype for each variant.

5

Interpretation

Interpretation of genotypes in light of the scientific evidence and the criteria defined for each variant.

6

Report preparation

Preparation of a personalised report on the genetic predispositions analysed, accompanied by the technical report and interpretative genetic counselling.

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THE INTERPRETATION MODEL

GENOMICA's interpretation model integrates the scientific evidence available for each marker. Sources include functional studies, candidate-gene and genome-wide association studies, prospective cohorts, systematic reviews and meta-analyses, as well as large population studies.

- **Functional studies**
- **Candidate-gene and genome-wide association studies**
- **Prospective cohorts**
- **Systematic reviews and meta-analyses**
- **Studies conducted on large population cohorts**

This approach provides a structured, biologically coherent interpretation of the genetic profile, to be considered alongside medical history, clinical findings, laboratory results and lifestyle.

Genetic profile + **Medical history** **Clinical findings** **Laboratory results** **Lifestyle**

PREGNANCYPROFILE provides information on genetic predispositions and does not constitute a diagnosis, prognosis or medical prescription. Any changes to diet, supplements, medication, physical activity or pregnancy management must be agreed with a qualified healthcare professional.

PREGNANCYPROFILE

FROM SAMPLE TO REPORT IN A FEW SIMPLE STEPS

1. Request the kit
2. Complete the documentation
3. Collect the sample
4. Send it to the laboratory
5. Receive the personalised report

TYPE OF SAMPLE

- **Buccal swab**

  or

- **Peripheral blood**

REPORT TURNAROUND TIME

approximately

10

working days

GENOMICA
Next Generation Genetics

Advanced genetics for more personalised medicine

GENOMICA is a laboratory and diagnostic centre specialising in medical genetics and molecular biology, working in both clinical applications and research. More than twenty years of professional experience and the use of advanced technologies support its commitment to accurate, reliable and accessible diagnostic services.

Available throughout **Italy** and **abroad**

Laboratories with **groundbreaking technologies** and high quality standards

Over **100.000 genetic tests/year**

Dedicated **R&D Team**

Team of medical **genetics specialists**

Professionals with **over 20 years of experience** in genetics and molecular biology

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