GENOMICA
Next Generation Genetics

Non-invasive maternal blood test for the identification of genetic causes of recurrent non-chromosomal spontaneous miscarriage

Analysis of circulating cell-free fetal DNA (cfDNA) by NGS

POCADVANCE
cfDNA Genetics

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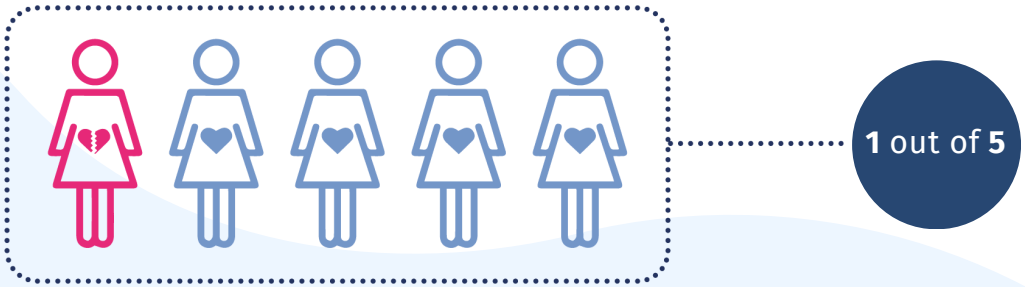
CLINICAL BACKGROUND

Spontaneous miscarriage is the most common complication in early pregnancy, with an estimated incidence of **15–25%** clinically recognized pregnancies. In the vast majority of cases, the event is attributable to **chromosomal abnormalities[1-2] of the products of conception (POC)**—and in these contexts, cytogenetic or cytogenomic analysis of the POC often provides a clinically conclusive answer.
But what happens when that answer does not come?Approximately **40%** of miscarriage events remain without an identified cause. Yet, in many cases, a cause does exist: **pathogenic variants** in genes involved in **embryo implantation**, **placental formation and function**, **maternal–fetal immune tolerance**, and **early embryonic development** may represent genetic determinants predisposing to recurrent pregnancy loss that are not captured by conventional investigations.



[1] D'Ippolito S. et al., 2017
[2] Rosenfeld J.A. et al., 2015

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THE POCADVANCE cfDNA GENETICS TEST

POCADVANCE cfDNA GENETICS is a **non-invasive** genetic test that, through analysis of **circulating cell-free fetal DNA** (**cfDNA**) from a maternal blood sample, investigates genetic determinants associated with **recurrent spontaneous miscarriage not attributable to a chromosomal abnormality**.

Advantages of cfDNA analysis

- **Non-invasive**: performed with a simple maternal blood draw
- **Clinically useful timing**: can be performed before any uterine evacuation procedure
- **Applicable early**: potentially feasible in the **early stages** of pregnancy (≥ 5 weeks)

CIRCULATING CELL-FREE FETAL DNA (cfDNA): BIOLOGICAL RATIONALE

During pregnancy, the placenta physiologically releases DNA fragments into the maternal circulation (apoptosis), starting from approximately the **5th week of gestation**. This material is defined as circulating **cell-free fetal DNA** (**cfDNA**).

Close to a miscarriage event, placental tissue may continue to release cfDNA into the maternal blood, making it possible to perform **non-invasive** investigations immediately after the ultrasound diagnosis of spontaneous pregnancy loss, with the aim of obtaining information useful on the potential genetic contribution.

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TWO LEVELS OF ANALYSIS

FOCUS

Targeted analysis of **19 genes** in which pathogenic variants have been associated with **non-chromosomal recurrent spontaneous pregnancy loss**.

Genes Analyzed			
NLRP7 (NALP7)	KHDC3L	SYCP3	HLA-G
WNT6	CEP250	CGB	NLRP10
PROKR1	FOXP3	OSBPL5	C4BPA
ANXA5	CD46	REC114	FOXD1
NLRP5	PADI6	TLE6	

EXOME

Clinical Exome Sequencing: sequencing of the coding regions of approximately **7,000 genes**, including genes known to be associated with pregnancy loss and related phenotypes.

Clinical relevance

Identification of a **pathogenic variant** in one of the analyzed genes suggests a possible genetic determinant associated with **recurrent spontaneous pregnancy loss** and may support more informed reproductive planning and **personalized counseling**.

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TECHNOLOGY: HIGH RESOLUTION AND ADVANCED BIOINFORMATICS

Blood withdraw | **cfDNA extraction** | **NGS sequencing** | **Bioinformatic analysis** | **Clinical interpretation of variants**

Key analytical features:

- **FOCUS**: full exon sequencing (whole-exon sequencing) of the panel genes
- **EXOME**: Clinical Exome Sequencing (~7.000 genes)
- Advanced pipeline for **variant detection**, **annotation**, and **prioritization**

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TEST RESULTS

POSITIVE

Pathogenic variant detected.
Clinical significance should be interpreted in the context of:

- reproductive and clinical history
- laboratory/instrumental findings
- cytogenetic/cytogenomic results

NEGATIVE

No pathogenic variant detected.
This does not exclude a genetic basis, as the cause may involve:

- genes not included in the panel (FOCUS level)
- variants in regions not investigated or not fully assessable
- non-genetic multifactorial determinants

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INDICATIONS FOR TESTING

POCADVANCE cfDNA GENETICS is particularly indicated in the following clinical settings:

- ✓ **spontaneous miscarriage** (anembryonic gestational sac, absence of cardiac activity, miscarriage in progress) when a timely, non-invasive investigation is desired;
- ✓ history of **recurrent pregnancy loss** with no identified chromosomal cause;
- ✓ **repeated pregnancy losses** in the absence of an exhaustive clinical explanation.

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HOW TO ORDER THE TEST

Kit request → **Documentation completion** → **Sample collection** → **Sample shipment** → **Report delivery**

Blood draw timing

The blood sample should be collected **as soon as possible** after ultrasound confirmation of pregnancy loss and **before** any uterine evacuation procedure; alternatively, **within 24 hours** of expulsion of the products of conception.

The test can be performed in **singleton or twin pregnancies** (monozygotic or dizygotic) at **≥ 5 weeks** of gestation.

Turnaround time **15 days**

GENOMICA
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Leading diagnostic laboratory and research center of excellence specializing in genetics and molecular diagnostics.

GENOMICA is a highly innovative company with extensive technical and scientific expertise, active in both clinical applications and research. Supported by a team with over 20 years of experience in molecular diagnostics, GENOMICA combines cutting-edge technology with a strong commitment to innovation, delivering increasingly accurate and accessible diagnostic services.

Over **100.000 genetic tests/year**

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

Dedicated **R&D Team**

International **Partnerships**

Personalized genetic counseling with genetic counselors experts in discussing genetic test results and familial risks

20+ years experience in prenatal molecular diagnostics

POCAdvance cfDNA Genetics ENG rev.00

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Visit the website dedicated to the test