GENOMICA
Next Generation Genetics

Advanced carrier screening integrated with couple infertility genetics

One test, four integrated clinical dimensions

- *Carrier screening*
- *Couple infertility genetics*
- *Probability of sperm retrieval in NOA*
- *Predisposition to embryonic aneuploidies*

www.carrieradvance.it

CARRIERADVANCE

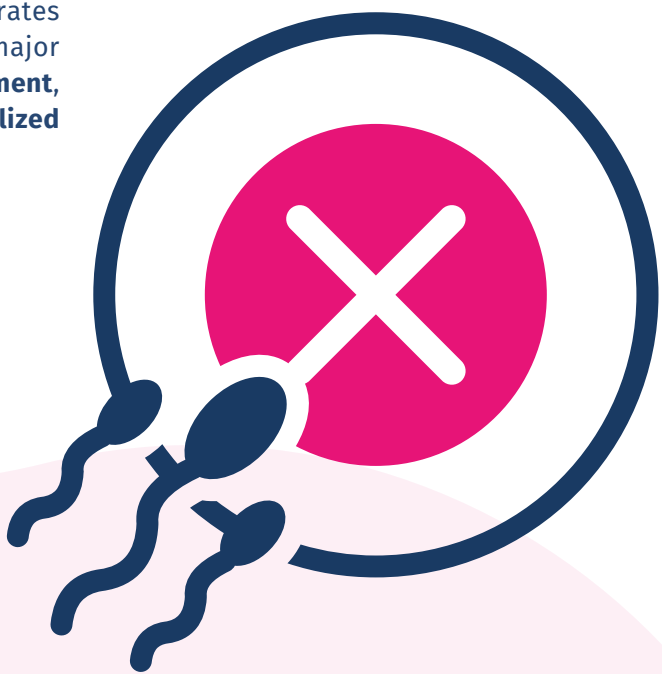
Exome Infertility

CARRIERADVANCE *Exome Infertility*

CLINICAL RATIONALE

Couple infertility affects approximately **15%** of the reproductive-age population. Genetic causes account for a substantial proportion of cases (**10–15%** in male infertility; **8–10%** in female infertility), while a meaningful share—around **20%**—remains **idiopathic** even after a complete diagnostic work-up.[1]

In this context, having a single platform that integrates **carrier screening** and **infertility genetics** represents a major step forward, enabling **optimized etiological assessment**, stronger **reproductive counseling**, and **more personalized assisted reproduction (ART) pathways**.



[1] Registro Nazionale PMA – Istituto Superiore di Sanità, Infertilità e tecniche di PMA, aggiornamento 09/03/2018.

CARRIERADVANCE *Exome Infertility*

FOUR CLINICAL DIMENSIONS IN A SINGLE ANALYSIS

CARRIERADVANCE Exome Infertility è is a genetic test designed for couples with reproductive difficulties who are planning a pregnancy through ART.

The test integrates, in one analysis, **four high-impact clinical areas**:

1 Expanded Carrier Screening

Clinical Exome Sequencing:

- **Clinical exome** sequencing of **7,000+ genes** associated with Mendelian disorders.
- Identification of the risk of transmitting genetic conditions to offspring, often **in the absence of a family history**.

2 Couple Infertility Genetics

- Diagnostic assessment of the main **genetic causes** of male and female infertility;
- Support in developing **personalized clinical strategies**.

3 TESE Prognosis in NOA

- Estimation of the likelihood of sperm retrieval in patients with **non-obstructive azoospermia (NOA).**
- Prognostic stratification **TESE+/TESE–** to support targeted clinical decisions.

4 Predisposition to Embryonic Aneuploidy

- Assessment of the risk of **meiotic** and **post-zygotic mitotic** errors.
- Useful in complex clinical scenarios (e.g., repeated implantation failure, recurrent pregnancy loss).

CARRIERADVANCE Exome Infertility

EXPANDED CARRIER SCREENING: 7,000+ GENETIC DISORDERS

CARRIERADVANCE Exome Fertility is among the most comprehensive **carrier screening** solutions currently available. Using **Clinical Exome Sequencing**, it analyzes the entire coding region of approximately **7,000 genes** associated with Mendelian disorders. The test identifies couples at risk of transmitting genetic diseases, frequently even in the absence of a family history.

Key elements for counseling

- Most carriers are clinically **asymptomatic** and often **unaware** of their carrier status.
- **Autosomal recessive inheritance**: if both partners carry pathogenic variants in the same gene, the risk of having an affected child is **25% per pregnancy**.
- **X-linked inheritance**: if the woman is a carrier, each male child has a **50%** risk of being affected.
- **Couple-based testing** maximizes clinical relevance and supports informed reproductive decisions (PGT-M, prenatal diagnosis, family counseling).

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COUPLE INFERTILITY GENETICS

CARRIERADVANCE Exome Infertility enables an integrated assessment of the main genetic conditions associated with male and female infertility, helping reduce the proportion of **idiopathic** infertility and guiding therapeutic strategy.

Female infertility

- Primary ovarian insufficiency (POI)
- Gonadal dysgenesis and ovarian dysfunction
- Oocyte maturation defects
- Oocyte aneuploidy / embryonic lethality
- Recurrent pregnancy loss (monogenic causes)

Male infertility

- Non-obstructive azoospermia (NOA)
- Severe asthenozoospermia
- Sperm morphological defects
- Genetically determined spermatogenic failure

Clinical value: support for etiological diagnosis, reproductive risk stratification, and definition of personalized pathways (ART, targeted PGT-M when indicated, family counseling).

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NOA AND PROGNOSTIC TESE STRATIFICATION

Non-obstructive azoospermia (**NOA**) is the most severe form of male infertility (prevalence **~1%** of the male population). In these patients, TESE/micro-TESE is often the only option to retrieve sperm usable for ICSI, with failure rates around **50%** in idiopathic cohorts. First-line genetic tests (karyotype, AZF microdeletions) provide limited prognostic value in most cases.

CARRIERADVANCE Exome Fertility analyzes **200+ genes** involved in key spermatogenic processes, enabling:

- Identification of the **molecular cause** of NOA/spermatogenic failure.
- **Prognostic stratification of TESE outcome** (**probability of sperm retrieval**) based on genes with evidence for **TESE−/TESE+**.[2]

TESE− (Unfavorable prognosis)

Pathogenic variants in genes consistently associated with **failed sperm retrieval**.
Clinica Utility: evaluate whether to avoid repeated invasive procedures with a poor risk/benefit ratio; redirect the couple toward alternative options.

TESE+ (Retrieval possible)

Pathogenic variants in genes compatible with residual spermatogenesis.
Clinical Utility:TESE/micro-TESE may be justified. Success remains gene-dependent and influenced by phenotype/histology; overall andrological assessment remains decisive.

[2] Riera-Escamilla et al. Genetic determinants of testicular sperm extraction outcomes: insights from a large multicentre study of men with non-obstructive azoospermia. Hum Reprod Open. 2025 Aug 29;2025(3):hoaf049.

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PREDISPOSITION TO EMBRYONIC ANEUPLOIDY

Numerical chromosomal **aneuploidies** are a major cause of implantation failure and early miscarriage in ART. They may originate from:

- **Meiotic errors:** predominantly maternal, influenced by biological age with possible individual genetic modulation.
- **Post-zygotic mitotic errors**: resulting in mosaicism and complex chromosomal patterns.

CARRIERADVANCE Exome Fertility analyzes **13 genes** selected on the basis of current scientific evidence to identify individual predisposition to:

- **Meiotic aneuploidies** (segregation errors in meiosis I/II).
- **Post-zygotic mitotic errors** (mosaicism, multiple aneuploidies, complex patterns).

The test **does not diagnose** embryonic aneuploidy; it provides an **individual risk-stratification tool** to be integrated with clinical phenotype, laboratory data, and previous investigations.

Carioscia et al. Nature 2026 doi: 10.1038/s41586-025-09964-2.
Sun et al. Am. J. Hum Genet 2023; 110:2092-2102;
Tyc et al. Hum Reprod. 2020 9;35:2134–2148.
Nguyen et al. Mol Hum Reprod 2017 13;23:406–416.
Biswas, et al. Proc. Natl. Acad. Sci. U.S.A.(2024) 121 (45) e2414963121.
Lledo et al. J Assist Reprod Genet . 2023;40:1755-1763.
McCoy et al. Science. 2015 10;348:235–238.

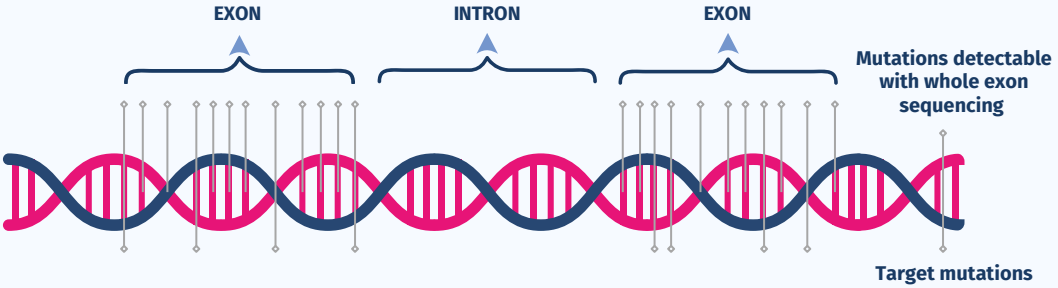
CARRIERADVANCE *Exome Infertility*

TECHNOLOGY PLATFORM

Sample collection | **DNA extraction** | **Next Generation Sequencing (NGS)** | **Detection of DNA mutations** | **Receive results**

CARRIERADVANCE Exome Fertility is based on **Clinical Exome Sequencing** using state-of-the-art NGS technology, sequencing the entire coding region of **~7,000 genes**. The integrated **advanced bioinformatics pipeline** enables detection of **SNVs**, **indels**, and **CNVs** in the investigated regions.

Advantage over targeted panels: no predefined mutation set; detection of any variant within the sequenced regions.



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REPORT INTERPRETATION

Carrier Screening & Infertility Genetics

POSITIVE: one or more variants identified (pathogenic or VUS).
Interpretation depends on the gene, inheritance mechanism, and clinical phenotype.

NEGATIVE: no relevant variants identified.
Clinical decisions rely on comprehensive evaluation.

TESE Prognosis / Aneuploidy Predisposition

POSITIVE: pathogenic variant identified.

- **NOA**: contributes to TESE+/TESE− prognostic stratification.
- **Aneuploidy**: may indicate increased predisposition (to be integrated with clinical data and PGT-A results).

NEGATIVE: no variants detected in the analyzed genes.
Does not fully exclude genetic risk (the test does not cover the entire genome).

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INDICATIONS FOR TESTING

The test is recommended in the presence of:

- **ART pregnancy** planning (preferred indication for the couple).
- **Idiopathic couple infertility.**
- **Donor conception**: genetic matching of donor/partner.
- Known or suspected **family history of genetic disease.**
- **Non-obstructive azoospermia (NOA)**: pre-TESE evaluation and post-negative TESE assessment.
- **Repeated implantation failures** without apparent cause.
- **Recurrent miscarriage**, particularly with evidence of embryonic aneuploidy.
- **High proportion of aneuploid embryos at PGT-A**, especially if unexpected for maternal age.
- ***PGT-A patterns suggestive of meiotic or mitotic errors*** *(multiple aneuploidies, mosaicism).*

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A SIMPLE, STEP-BY-STEP WORKFLOW

Kit request

Completion of kit documentation

Sample collection

Sample shipment

Report delivery

Turnaround time **20 days**

GENOMICA
Next Generation Genetics

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

CarrierAdvance Exome Infertility ENG rev.00

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Visit the website dedicated to the test