GENOMICA
Next Generation Genetics

# The first non-invasive prenatal test that screens for genetic diseases associated with autism spectrum disorders

- Genetic diseases associated with ASD
- Inherited and de novo genetic disorders
- Common and rare chromosomal aneuploidies
- Segmental chromosomal abnormalities
- Microdeletion / microduplication syndromes
- Microdeletions / microduplications associated with ASD
- Fetal RhD and Fetal gender

www.prenatalautism.it

PRENATALAUTISM

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## AUTISM SPECTRUM DISORDERS

**Autism Spectrum Disorders** (**ASD**) represent a heterogeneous group of neurodevelopmental conditions characterized by altered maturation and connectivity of brain networks.
From a clinical perspective, ASD is typically characterized by:

- **Persistent impairment in communication and social interaction,** which may manifest as difficulties in verbal and non-verbal language, understanding others' emotions, and social reciprocity.

- **The presence of restricted, repetitive, and stereotyped behaviors and interests,** which may include rituals, insistence on sameness, repetitive movements, or an intense focus on specific objects or topics.

Common comorbidities include:

- **Intellectual disability** (**≈30–40%** of cases);
- **Language disorders;**
- **Epilepsy** (**affecting up to 20–30%** of individuals);
- **Sleep and behavioral disorders.**

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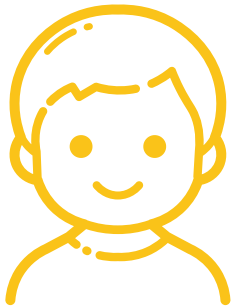
## INCIDENCE OF CONDITIONS ASSOCIATED WITH AUTISM SPECTRUM DISORDERS

The prevalence of ASD has increased over the past decades, partly due to the broadening of diagnostic criteria and greater clinical and social awareness. It is estimated that more than **1 in 100 children** are affected by an autism spectrum disorder. In Italy, according to data from the Istituto Superiore di Sanità, approximately **1 in 77 children** aged 7 to 9 receive an ASD diagnosis, with a markedly higher prevalence in **males**, who are about **4.4 times more likely to be affected** compared to females.[1].



**1** in **100**

**ASD DIAGNOSIS**

1. Istituto Superiore di Sanità. Disturbi dello spettro autistico nei bambini e negli adolescenti. Linea guida 2023.

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## GENETIC BASIS OF AUTISM SPECTRUM DISORDERS

Scientific evidence indicates that **genetic factors** play a **predominant role** in the development of autism, accounting for approximately **70–90%** of cases.[2-3]

Genetic abnormalities may include:

- **Point mutations** or **pathogenic variants** in key genes involved in neuronal development, synaptogenesis, and synaptic transmission (e.g., CHD8, SCN2A, SHANK3, SYNGAP1). [4-5]
- **Copy Number Variants** (**CNVs**), i.e., **microdeletions** or **microduplications** of chromosomal regions, such as those located on 16p11.2 or 15q13.3.
- **Genetic syndromes associated with autism,** including tuberous sclerosis, Rett syndrome, and Phelan-McDermid syndrome, which account for a significant proportion of syndromic ASD cases.[6-7]


2. Tick B et al. Heritability of autism spectrum disorders: a meta-analysis of twin studies. JAMA Psychiatry. 2016;73(3): 258-268.
3. Sandin S et al. The familial risk of autism. JAMA. 2014;311(17):1770-1777.
4. Satterstrom FK et al. Large-Scale Exome Sequencing Study Implicates Both Developmental and Functional Changes in the Neurobiology of Autism. Cell. 2020;180(3):568-584.e23.
5. Iossifov I et al. The contribution of de novo coding mutations to autism spectrum disorder. Nature. 2014;515:216-221.
6. Rolland T, et al. Phenotypic effects of genetic variants associated with autism Nat Med. 2023 Jul;29(7):1671-1680.
7. Grove J et al. Identification of common genetic risk variants for autism spectrum disorder. Nat Genet. 2019;51:431-444.

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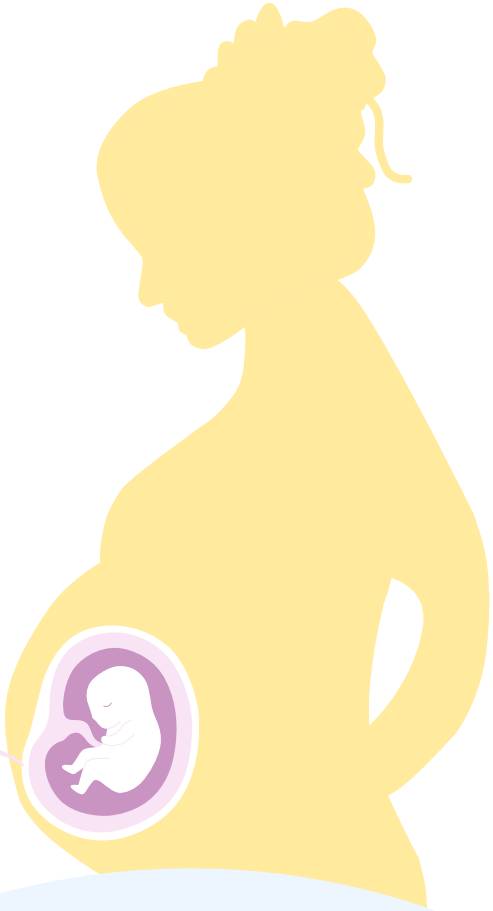
An advanced non-invasive prenatal screening test that analyzes **circulating cell-free fetal DNA** (**cfDNA**) from a maternal blood sample to identify fetal mutations responsible for severe genetic diseases associated with **Autism Spectrum Disorders**. This state-of-the-art approach offers superior accuracy and detection capabilities compared to conventional NIPTs.

During pregnancy, the placenta releases DNA fragments into the maternal bloodstream via a physiological process known as "apoptosis", starting from the 5th week of gestation.

The quantity of this DNA, also named **circulating cell-free fetal DNA**, increases as the pregnancy progresses, reaching levels sufficient for reliable analysis by the 10th week, providing valuable insights into the fetus's health.

PRENATALAUTISM

## 3 LEVELS OF SCREENING DESIGNED TO MEET THE NEEDS OF EVERY PREGNANCY

### 1 PRENATALAUTISM *Basic*

Screening for **300+ genetic diseases** associated with **Autism Spectrum Disorders** (**ASD**).

### 2 PRENATALAUTISM *Karyo*

Screening for **300+ genetic diseases associated with ASD**.
The test also allows the detection of:

- Common and rare **chromosomal aneuploidies**;
- Segmental **deletions** and **duplications**;
- **130+ microdeletion/microduplication** syndromes;
- **23** specific **microdeletions/microduplications associated with ASD**.

### 3 PRENATALAUTISM *Genetics*

Provides the most comprehensive level of screening, enabling the investigation of the fetus for:

- **300+ genetic diseases associated with ASD**;
- **1000+** of the most common **inherited genetic disorders**;
- **1000+ de novo genetic conditions**.
- Common and rare **chromosomal aneuploidies;**
- Segmental **deletions** and **duplications;**
- **130+ microdeletion/microduplication** syndromes;
- **23** specific **microdeletions/microduplications associated with ASD.**

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## COMPARING THE SCREENING OPTIONS

| PrenatalAutism | N° | Basic | Karyo | Genetics |
|---|---|---|---|---|
| Genetic diseases associated with ASD | **300+** | ✓ | ✓ | ✓ |
| *De novo* genetic conditions | **1000+** | | | ✓ |
| Common inherited genetic disorders | **1000+** | | | ✓ |
| Common and rare chromosomal aneuploidies | **24 Chromosomes** | | ✓ | ✓ |
| Segmental deletions and duplications | **> 7Mb** | | ✓ | ✓ |
| Microdeletion/microduplication syndromes | **130+** | | ✓ | ✓ |
| Specific microdeletions/microduplications associated with ASD | **23** | | ✓ | ✓ |

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## DETAILED OVERVIEW OF TEST FINDINGS

→ **1000+** INHERITED GENETIC DISORDERS

→ **1000+** DE NOVO GENETIC CONDITIONS

→ **300+** GENETIC DISEASES ASSOCIATED WITH ASD

The complete list of genetic diseases can be accessed by scanning the QR Code.

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# DETAILED OVERVIEW OF TEST FINDINGS

## 24 FETAL KARYOTYPE SCREENING

Screening for common and rare fetal aneuploidies, segmental deletions and duplications[§] across the whole fetal genome, providing karyotype-level insight

**§ >7 Mb**

**Common chromosomal aneuploidies**

| | | | |
|---|---|---|---|
| Trisomy 21 | Trisomy 18 | Trisomy 13 | |
| Monosomy X | XXX | XXY | XYY |

**Rare chromosomal aneuploidies**

| | | | |
|---|---|---|---|
| Trisomy 1 | Trisomy 2 | Trisomy 3 | Trisomy 4 |
| Trisomy 5 | Trisomy 6 | Trisomy 7 | Trisomy 8 |
| Trisomy 9* | Trisomy 10 | Trisomy 11 | Trisomy 12 |
| Trisomy 14 | Trisomy 15 | Trisomy 16* | Trisomy 17 |
| Trisomy 19 | Trisomy 20 | Trisomy 22* | |

*With higher incidence among the less common fetal aneuploidies

## >130 MICRODELETION/MICRODUPLICATION SYNDROMES

As low as 1 Mb

## 23 SPECIFIC MICRODELETIONS/MICRODUPLICATIONS

Associated with Autism Spectrum Disorders

**The complete list of microdeletion/microduplication syndromes can be accessed by scanning the QR Code**

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## A GROUNDBREAKING TECHNOLOGY FOR REVOLUTIONARY SCREENING

The advanced **high-resolution fetal genome sequencing** technology[8-9], combined with sophisticated **bioinformatic analysis** using a proprietary algorithm, enables the study of the fetal karyotype and the screening of **hundreds of severe genetic disorders** in the fetus, including those associated with **Autism Spectrum Disorders**, **inherited** conditions, and ***de novo*** diseases, in a single analysis. This level of detail was previously achievable only through invasive prenatal diagnostic methods.

1

**CfDNA extraction**

2

**Library prep and exome capture**

3

**Deep fetal exome sequencing by *Next Generation Sequencing* (>500X)**

8. Brand H, Whelan CW, Duyzend M, et al. High-resolution and noninvasive fetal exome screening. N Engl J Med. 2023;389:2014-2016.
9. Miceikaitė I, Hao Q, Brasch-Andersen C, et al. Comprehensive Noninvasive Fetal Screening by Deep Trio-Exome Sequencing. N Engl J Med. 2023;389:2017-2019.

4

**Screening for chromosomal aneuploidies and structural aberrations**

5

**CfDNA mutation analysis**

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The high resolution of the test allows for a low limit of detection (LOD)

**Highly accurate at** **1%** of **Fetal Fraction**

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## THE TEST REPORT

The test result may be **negative**, indicating a low risk for a chromosomal abnormality or a genetic disease in the fetus. In such cases, the pregnancy may proceed without any need for follow-up.

In some cases, the test result may be **positive**, indicating a higher risk for a chromosomal abnormality or a genetic disease in the fetus.
Such instances require **follow-up with invasive prenatal diagnostic techniques** (amniocentesis or chorionic villus sampling) to confirm the findings.

### Follow-Up for Positive Results

Amniocentesis or chorionic villus sampling to confirm the detected chromosomal anomaly or genetic disease.

### Complimentary services

- *Refund in cases of entirely inconclusive test results;*
- *Free Pre- and Post-test genetic counseling.*

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# A TEST THAT MEETS THE HIGHEST QUALITY STANDARDS

### SIMPLE
A simple blood sample collected at 10^ weeks of gestation is required

### RELIABLE
Sensitivity and specificity >99%

### SENSITIVE
Low limit of detection: highly accurate at low cfDNA quantity (FF:1%)

### COMPLETE
Detection of both genome-wide chromosomal abnormalities and single gene disorders, providing the most comprehensive information available from a non-invasive prenatal test to date

### ADVANCED
Groundbreaking technologies and advanced bioinformatic analysis

### VALIDATED
Pre-clinical validation studies performed on a wide cohort of pregnant women

# INDICATION FOR TESTING PRENATALAUTISM

## SUITABLE FOR ANY PREGNANCY

- Pregnant women under and over 35 years of age
- Contraindication to invasive prenatal diagnosis (amniocentesis, chorionic villus sampling)
- Singleton and twin pregnancies, whether conceived naturally or through autologous or heterologous assisted reproductive technologies
- Pregnancies with abnormal ultrasound findings
- Pregnant women wishing to reduce the risk of fetal genetic diseases associated with ASD
- Family history of chromosomal aneuploidy or genetic disease
- Couples in which the male partner is of advanced paternal age, a condition associated with an increased risk of *de novo* mutations
- Patients with a known risk of transmitting to the fetus a genetic disease detectable by the test

**PrenatalAutism represents the ideal solution to provide in-depth and personalized information, tailored to the needs of each couple.**

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## HOW TO PERFORM THE TEST

1. Request the shipping kit
2. Fill in the test requisition form
3. Collect blood samples
4. Ship the samples to Genomica
5. Receive results

## SAMPLES REQUIRED

**MATERNAL SAMPLE**

Peripheral blood sample
(2 Streck tubes)

**PATERNAL SAMPLE**

Buccal Swab or Blood in EDTA tube
(the paternal sample is optional)

## TURNAROUND TIME

**CHROMOSOMAL ANEUPLOIDIES**

3
working days
(selecting the rapid reporting option)

**GENETIC DISORDERS**

15
working days

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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

PrenataAutism ENG M rev.00


**LABORATORIES**

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Visit the website dedicated to the test