GENOMICA
Next Generation Genetics

The most advanced cell-free fetal DNA-based non-invasive prenatal test

- Common and rare chromosomal aneuploidies
- Segmental chromosomal abnormalities
- Microdeletion syndromes
- Inherited and de novo genetic disorders
- Fetal RhD
- Fetal gender
- Parental carrier screening

PRENATALADVANCE
NON INVASIVE PRENATAL TEST (NIPT)

www.prenataladvance.com

PRENATALADVANCE
NON INVASIVE PRENATAL TEST (NIPT)

THE NEXT GENERATION NIPT

The most advanced non-invasive prenatal test (NIPT) that uses groundbreaking technologies. Through analysis of circulating cell-free fetal DNA (cfDNA) in maternal blood, it screens for genome-wide chromosomal abnormalities and severe genetic disorders in the fetus, providing unparalleled accuracy and detection compared to other NIPT

During pregnancy placental trophoblasts, through a physiological process known as "apoptosis", releases DNA fragments in the maternal blood.

This DNA, also named circulating cell-free fetal DNA, increases with advancing of gestational age and, at the 10th week of gestation, reaches a sufficient quantity for a reliably analysis and provides valuable information on the health of the fetus.

INDICATION FOR TESTING

PRENATALADVANCE
NON INVASIVE PRENATAL TEST (NIPT)

SUITABLE TO EVERY PREGNANCY

- Maternal age-related risks (≥35 years)
- Low risk pregnancies
- Singleton or twin pregnancy, IVF derived or naturally conceived pregnancy,
- Positive results on maternal serum screening
- Pregnancy at risk for a de novo or inherited genetic disorder
- Prior pregnancy with a chromosomal abnormality
- Carrier of a balanced chromosomal translocation
- Low risk pregnancies

The test is suitable for every kind of pregnancy: singleton or twin pregnancy, natural conception or IVF derived pregnancy, pregnancy at risk for an inherited genetic disorder or to any pregnancy without a specific a priori risk.

PRENATALADVANCE
NON INVASIVE PRENATAL TEST (NIPT)

A CUTTING-EDGE NIPT THAT

STANDARD TESTS
FOR SCREENING OF COMMON FETAL ANEUPLOIDIES

PRENATALADVANCE 3
NON INVASIVE PRENATAL TEST (NIPT)

Aneuploidy Screening on chromosomes 13, 18, 21 and fetal gender determination.

PRENATALADVANCE 5
NON INVASIVE PRENATAL TEST (NIPT)

Aneuploidy Screening on chromosomes 13, 18, 21, X, Y and fetal gender determination.

PRENATALADVANCE +
NON INVASIVE PRENATAL TEST (NIPT)

Aneuploidy Screening on chromosomes 13, 18, 21, X, Y and on chromosomes 9, 16, 22 and fetal gender determination. It also includes screening for 9 common microdeletion syndromes.

COMPARISON OF THE SCREENING OPTIONS

PrenatalAdvance	3	5	+	K	K+	G	M	G+
Common aneuploidies	●	●	●	●	●	●	●	●
Rare aneuploidies			●	●	●	●	●	●
Fetal gender	●	●	●	●	●	●	●	●
Fetal RhD	●	●	●	●	●	●	●	●
Genome-wide screening				●	●	●	●	●
Screening of microdeletion syndromes			●		●		●	●
Segmental chromosomal abnormalisties (deletions/duplications)				●	●	●	●	●
Unbalanced chromosomal translocations				●	●	●	●	●
Inherited genetic disorders						●	●	●
De-novo genetic disorders						●	●	●
Parental carrier screening								●

OFFERS A FULL PANEL OF SCREENING OPTIONS

ADVANCED TESTS FOR GENOME-WIDE SCREENING OF FETAL CHROMOSOMAL ABNORMALITIES AND GENETIC DISORDERS

PRENATALADVANCE GENOME-WIDE NON-INVASIVE PRENATAL TEST K *Karyo*

Screening for aneuploidies and structural chromosomal aberrations (deletions or duplications) accross the fetal genome, providing karyotype-level insight. It includes fetal gender determination.

PRENATALADVANCE GENOME-WIDE NON-INVASIVE PRENATAL TEST K+ *Karyo Plus*

Screening for aneuploidies and structural chromosomal aberrations (deletions or duplications) accross the fetal genome, providing karyotype-level insight. It includes also screening for 50 microdeletion / microduplication syndromes and fetal gender determination.

PRENATALADVANCE GENOME-WIDE NON-INVASIVE PRENATAL TEST G *Genetics*

Screening for aneuploidies and structural chromosomal aberrations (deletions or duplications) accross the fetal genome, providing karyotype-level insight. It also includes screening for severe genetic disorders, 26 inherited and 50+ de novo onset, and fetal gender determination. The test includes parental carrier screening

PRENATALADVANCE GENOME-WIDE NON-INVASIVE PRENATAL TEST M *Genetics Micro*

Screening for aneuploidies and structural chromosomal aberrations (deletions or duplications) accross the fetal genome, providing karyotype-level insight. It also includes screening for severe genetic disorders, 26 inherited and 50+ de novo onset, 50 microdeletion / microduplication syndromes and fetal gender determination.

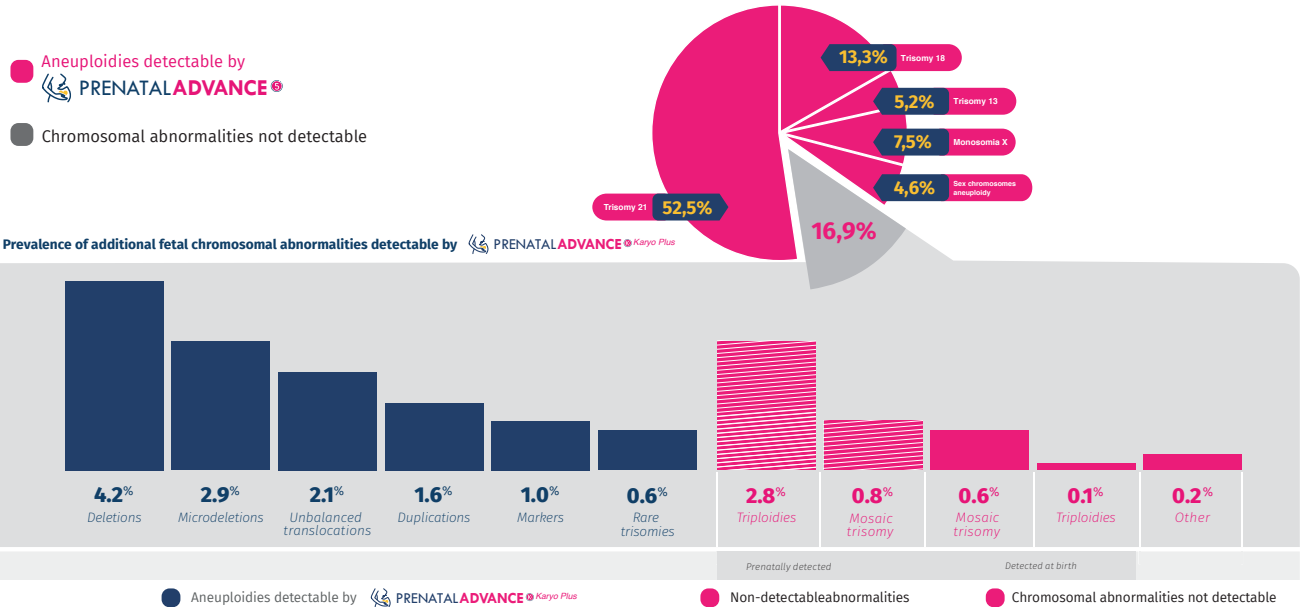
PRENATALADVANCE GENOME-WIDE NON-INVASIVE PRENATAL TEST G+ *Genetics Plus*

Screening for aneuploidies and structural chromosomal aberrations (deletions or duplications) accross the fetal genome, providing karyotype-level insight. It also includes screening for severe genetic disorders, 26 inherited and 50+ de novo onset, 50 microdeletion / microduplication syndromes and fetal gender determination. The test includes parental carrier screening.

PRENATALADVANCE Karyo Plus
GENOME-WIDE NON-INVASIVE PRENATAL TEST

DETECTS 99.1% OF CHROMOSOMAL ABNORMALITIES OBSERVED AT BIRTH[1]

PrenatalAdvance Karyo Plus test couples leading technology with unparalleled insight to offer the most advanced noninvasive prenatal test. Unlike any other NIPT available to date, focusing only on detection of common aneuploidies, it screens every chromosome in the fetal genome, providing information previously only available from a fetal karyotype analysis. PrenatalAdvance Karyo Plus can also detect, accross the fetal genome, other chromosomal abnormalities that may go undiagnosed, such as structural chromosomal aberrations (deletions or duplications), rare aneuploidies (e.g. trisomy 9,16, 22) and 50 microdeletions / microduplications sindromes.



1. Wellesley et al. Rare chromosome abnormalities, prevalence and prenatal diagnosis rates from population-based congenital anomaly registers in Europe. EurJHumGenet. 2012; 20: 521-526

PRENATALADVANCE
GENOME-WIDE NON-INVASIVE PRENATAL TEST
Karyo Plus

Microdeletion/Microduplication syndromes screened

MICRODELETION/MICRODUPLICATION SYNDROMES	CYTOGENETIC LOCATION
22q11 deletion syndrome (Velocardiofacial / DiGeorge syndrome)	22q11.2
22q11 duplication syndrome	22q11.2
Cri du Chat Syndrome (5p deletion)	5p15.3
Prader-Willi syndrome (Type 1)	15q11.2-q13.1
Angelman syndrome (Type 1)	15q11.2-q13.1
Prader-Willi Syndrome (Type 2)	15q11.2-q13.1
Angelman syndrome (Type 2)	15q11.2-q13.1v
1p36 microdeletion syndrome	1p36
Wolf-Hirschhorn syndrome (4p16.3 deletion syndrome)	4p16.3
Jacobsen syndrome (11q deletion syndrome)	11q23.3-q24.3
Langer-Giedion syndrome (8q24.1 deletion syndrome)	8q24.11-q24.13
Smith-Magenis Syndrome	17p11.2
Potocki-Lupski syndrome (17p11.2 duplication syndrome)	17p11.2
16p11.2-p12.2 microdeletion syndrome	16p11.2-p12.2
2q33.1 deletion syndrome	2q33.1
16p11.2-p12.2 microduplication syndrome	16p11.2-p12.2
8p23.1 deletion syndrome	8p23.1
8p23.1 duplication syndrome	8p23.1
12q14 microdeletion syndrome	12q14
Miller-Dieker microdeletion syndrome (MDS)	17p13.3
2p15-16.1 microdeletion syndrome	2p15-p16.1
Potocki-Shaffer microdeletion syndrome	11p11.2
18q deletion syndrome	18q22.3-q23
Witteveen-Kolk syndrome (15q24 Deletion)	15q24.2
Rubinstein-Taybi deletion syndrome (16p13.3 deletion syndrome)	16p13.3

PRENATALADVANCE
GENOME-WIDE NON-INVASIVE PRENATAL TEST
Karyo Plus

Microdeletion/Microduplication syndromes screened

MICRODELETION/MICRODUPLICATION SYNDROMES	CYTOGENETIC LOCATION
1q41-q42 deletion syndrome	1q41-q42
1q43-q44 deletion syndrome	1q43-q44
Glass syndrome (2q32-q33 deletion syndrome)	2q32-q33
17q23.1-q23.2 deletion syndrome	17q23.1-q23.2
2q23.1 microdeletion syndrome	2q23.1
6q25 microdeletion syndrome	6q25.2-q25.3
Phelan-McDermid syndrome (22q13.3 deletion syndrome)	22q13
19q13.11 deletion syndrome	19q13.11
17p13.3 duplication syndrome	17p13.3
3q13.31 deletion syndrome	3q13.31
8q22.1 deletion syndrome	8q22.1
14q22 deletion syndrome (Frias syndrome)	14q22.1-q22.3
1p32-p31 Deletion Syndrome	1p32-p31
5q12 deletion syndrome	5q12
15q25 deletion syndrome	15q25.2-q25.3
Yuan-Harel-Lupski syndrome (17p12-p11.2 duplication)	17p12-p11.2
4q21 deletion syndrome	4q21.1-q22.2
5q14.3 deletion syndrome	5q14.3-q15
2p12-p11.2 deletion syndrome	2p12-p11.2
10q26 deletion syndrome	10q26
3pter-p25 deletion syndrome	3pter-p25
6q24-q25 deletion syndrome	6q24-q25
Kleefstra syndrome (9q34.3 deletion syndrome)	9q34.3
2q37 deletion syndrome	2q37.2
17p13.1 deletion syndrome	17p13.1

PRENATALADVANCE Genetics Plus
GENOME-WIDE NON-INVASIVE PRENATAL TEST

THE NEXT LEVEL IN NON-INVASIVE PRENATAL TESTING

PrenatalAdvance Genetics represents the evolution of non-invasive prenatal tests and provides the most comprehensive information available from a NIPT to date. It works as a complementary test to standard and genome-wide PrenatalAdvance tests, screening not only for common aneuploidies and genome-wide chromosomal abnormalities, but also for severe genetic disorders in the fetus, allowing a more complete picture of the risk of a pregnancy being affected by a genetic disease. PrenatalAdvance Genetics facilitates early diagnosis of common single-gene disorders, allowing detection in the fetus of genetic disorders, 26 inherited and 50+ de novo onset, that could be missed by traditional prenatal screening. The test includes parental carrier screening.

Inherited genetic disorders screened in the fetus

GENE	GENETIC DISORDER
ACADM	Acyl-CoA dehydrogenase, medium chain deficiency
AGXT	Hyperoxaluria, primary, type 1
ARSA	Metachromatic leukodystrophy
ATP7B	Wilson disease
BTD	Biotinidase deficiency
CBS	Homocystinuria
CFTR	Cystic Fibrosis
DHCR7	Smith-Lemli-Opitz syndrome
EMD	Emery-Dreifuss muscular dystrophy 1
GAA	Glycogen storage disease II
GALC	Krabbe disease
GALT	Galactosemia
GBA	Gaucher disease, type I, II, III, IIIC, perinatal lethal

GENE	GENETIC DISORDER
GJB2	Deafness, autosomal recessive 1A
GJB6	Deafness, autosomal recessive 1B
GLA	Fabry disease
HADHA	Long chain 3-hydroxyacyl-CoA dehydrogenase deficiency
HBB	Beta thalassemia/Sickle cell anemia
HEXA	Tay-Sachs disease
MEFV	Familial Mediterranean fever
MMACHC	Methylmalonic aciduria and homocystinuria, cblC type
PAH	Phenylketonuria
PMM2	Congenital disorder of glycosylation, type Ia
SERPINA1	Alpha 1 antitrypsin deficiency
SLC26A2	Achondrogenesis Ib
GJB1	Charcot-Marie-Tooth neuropathy, X-linked dominant, 1

The inherited genetic disorders screened by PrenatalAdvance Genetics are the most common in the European population

PRENATALADVANCE
GENOME-WIDE NON-INVASIVE PRENATAL TEST
Genetics Plus

IDENTIFIES FETAL CONDITIONS THAT COULD BE MISSED BY TRADITIONAL PRENATAL SCREENING

De novo genetic conditions screened in the fetus

GENE	SYNDROMIC DISORDERS
ACTB	Baraitser-Winter syndrome
ACTG1	Baraitser-Winter syndrome
ASXL1	Bohring-Opitz syndrome
CHD7	CHARGE syndrome
HDAC8	Cornelia de Lange syndrome 5
JAG1	Alagille syndrome
MECP2	Rett syndrome
NIPBL	Cornelia de Lange syndrome 1
NSD1	Sotos syndrome 1
SETBP1	Schinzel-Giedion syndrome
SHH	Holoprosencephaly type 3
SOX9	Acampomelic campomelic dysplasia
ZIC2	Holoprosencephaly type 5

GENE	CRANIOSYNOSTOSIS
FGFR2	Antley-Bixler syndrome without genital anomalies or disordered steroidogenesis
	Apert syndrome
	Crouzon syndrome
	Jackson-Weiss syndrome
	Pfeiffer syndrome type 1
	Pfeiffer syndrome type 2
	Pfeiffer syndrome type 3

PrenatalAdvance Genetics test detects de novo mutations in 35 genes causing 56 different genetic disorders. The genetic conditions screened by this innovative test often occur in the absence of a family history of the condition. This is a paradigm shift in prenatal screening. PrenatalAdvance Genetics screens for de novo mutations that cannot be detected by standard carrier screening, as these mutations are not present on the parents. The genetic disorders screened by PrenatalAdvance Genetics can cause skeletal dysplasias, cardiac defects, multiple congenital anomalies, autism, epilepsy and/or intellectual disability.

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De novo genetic conditions screened in the fetus

GENE	SKELETAL DISORDERS
COL2A1	Achondrogenesis 2
FGFR3	Achondroplasia
	CATSHL syndrome
	Crouzon syndrome with acanthosis nigricans
	Hypochondroplasia
	Muenke syndrome
	Thanatophoric dysplasia, type I
	Thanatophoric dysplasia, type II
COL1A1	Ehlers-Danlos syndrome, classic
	Ehlers-Danlos syndrome, type VIIA
	Osteogenesis imperfecta, type I
	Osteogenesis imperfecta, type II
	Osteogenesis imperfecta, type III
	Osteogenesis imperfecta, type IV
COL1A2	Ehlers-Danlos syndrome, cardiac valvular form
	Ehlers-Danlos syndrome, type VIIB
	Osteogenesis imperfecta, type II
	Osteogenesis imperfecta, type III
	Osteogenesis imperfecta, type IV

GENE	NOONAN SYNDROME
BRAF	Cardiofaciocutaneous syndrome 1
CBL	Noonan syndrome-like disorder with or without juvenile myelomonocytic leukemia (NSLL)
HRAS	Costello syndrome/Noonan syndrome
KRAS	Noonan syndrome/cancers
MAP2K1	Cardiofaciocutaneous syndrome 3
MAP2K2	Cardiofaciocutaneous syndrome 4
MRAS	Noonan syndrome 11
NRAS	Noonan syndrome 6/cancers
PPP1CB	Noonan syndrome-like disorder with loose anagen hair 2
PTPN11	juvenile myelomonocytic leukemia (JMML)
PTPN11	Noonan syndrome 1/ LEOPARD syndrome/cancers
RAD21	Cornelia de Lange syndrome 4
RAF1	Noonan syndrome 5/LEOPARD syndrome 2
RIT1	Noonan syndrome 8
RRAS2	Noonan syndrome 12
SHOC2	Noonan syndrome-like disorder with loose anagen hair
SOS1	Noonan syndrome 4

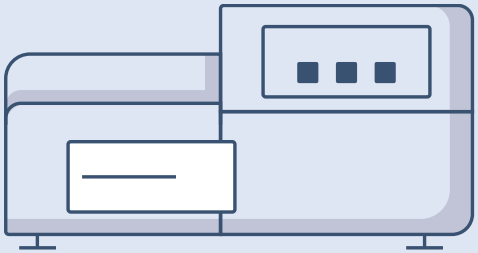
PRENATAL**ADVANCE**
NON INVASIVE PRENATAL TEST (NIPT)

A GROUNDBREAKING TECHNOLOGY ALLOWING FOR A SCREENING TEST THAT IS REVOLUTIONARY

A groundbreaking technology coupled with an advanced bioinformatic analysis allows for detection of both genomewide chromosomal abnormalities and single-gene disorders, providing the most comprehensive information available from a noninvasive prenatal test to date

CfDNA extraction

Frtal fraction determination



Next Generation Sequencing (NGS)

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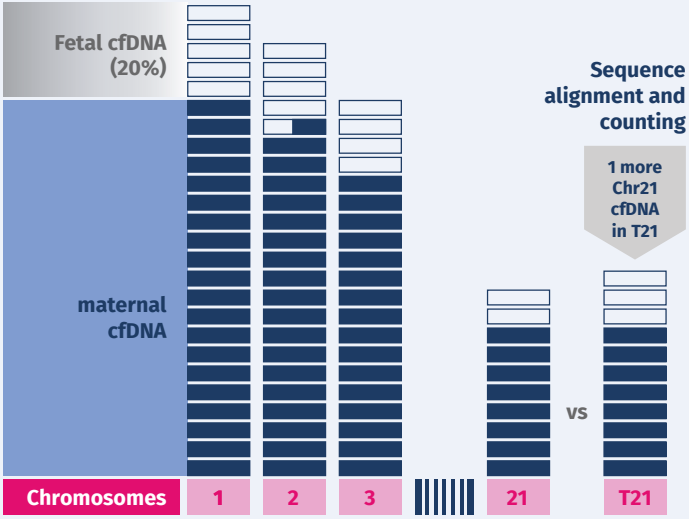
The high resolution of the test allows for a low limit of detection (LOD): highly accurate at low cfDNA quantity

LOD 1% Fetal Fraction

Screening for chromosomal aneuploidy and structural aberrations



CfDNA mutation analysis

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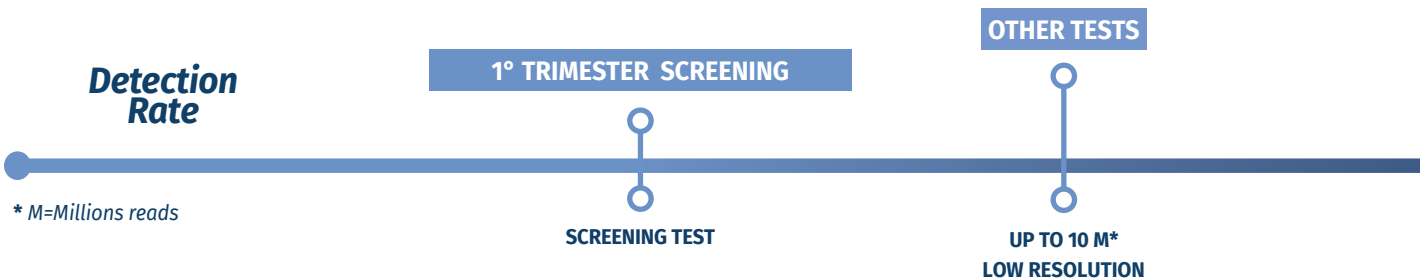
HIGH RESOLUTION



* *M=Millions reads*

VANTAGES OF USING A

HIGHER SENSITIVITY

- Increased detection rate
- Lower incidence of false negative

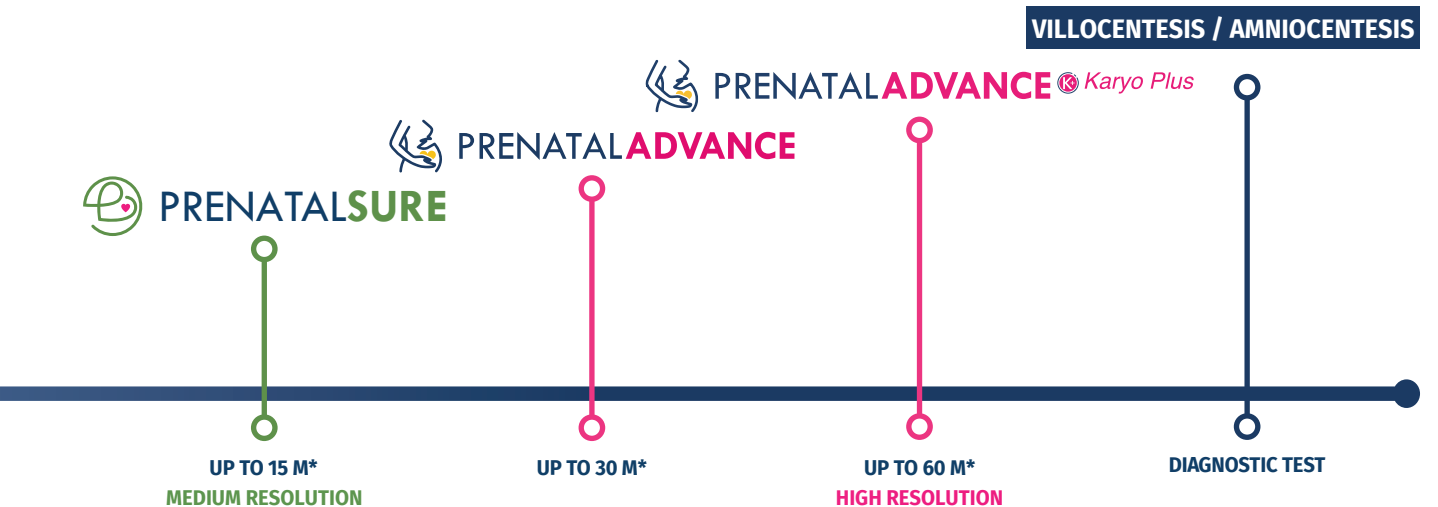
HIGHER SPECIFICITY

- Lower incidence of false positive
- Reduction of the number of invasive Prenatal Diagnosis

MICRODELETION SYNDROMES AND SEGMENTAL IMBALANCES

- Detection of microdeletions down to 2Mb
- Improved performance in detecting segmentals
- Increased detection rate
- Lower incidence of false negative and positive
- Riduzione dei falsi positivi

= BETTER PERFORMANCE



HIGH RESOLUTION NIPT

RELIABLE RESULTS AT LOW FF

- Increased detection rate at low FF
- Lower redraw incidence
- Idea test for patient with high BMI

MOSAICISM

- Detection of placental/fetal mosaicism
- Lower incidence of false positive

IMPROVED SEQUENCING DATA QUALITY

- Lower incidence of non-conclusive results
- Lower redraw rate
- Ideal for patients using interfering drugs

PRENATAL**ADVANCE**
NON INVASIVE PRENATAL TEST (NIPT)

TEST CHARACTERISTICS:

SIMPLE

A simple blood sample (8-10 ml) collected at 10^ weeks of gestation is required

FAST

Turnaround time of just 3 days

SAFE

It is a non-invasive prenatal test, no risk for the fetus and the mother

SENSITIVE

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

RELIABLE

Sensitivity and specificity >99%

COMPREHENSIVE

It offers a level of information previously only available from a fetal karyotype analysis, performed with invasive prenatal diagnosis procedures (amniocentesis and CVS)

SUPERIOR ACCURACY AND HIGH QUALITY STANDARDS

COMPLETE

It detects both genome-wide chromosomal abnormalities and single-gene disorders, providing the most comprehensive information available from a noninvasive prenatal test to date

ADVANCED

Groundbreaking technologies and advanced bioinformatic analysis

CERTIFICATED

CE-IVD marking for instruments, reagents and analysis algorithm

ITALIAN

Performed in Italy

VALIDATED

Clinical validation studies performed on a wide cohort of pregnant women

GLOBAL

It is used from thousands of gynecologists worldwide

TEST RESULTS

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NEGATIVE: A negative result shows that there is a low risk for a chromosomal abnormality or a genetic disorder in the fetus.
A low risk test result greatly reduces the chances that the fetus has a chromosomal abnormalty or monogenic disorder but it cannot guarantee a healthy baby.

POSITIVE: Positive screening result shows that there is a high risk for a chromosomal abnormality or a genetic disorder in the fetus. A patient with a positive test result should be referred for genetic counseling and should always be **followed-up** with an invasive diagnostic prenatal test for confirmation of test results, before any medical decisions are made.

COMPLIMENTARY SERVICES

- Reimbursement of the test fee for cases with inconclusive test results
- Pre- and Post-test genetic counseling
- Free **RhAdvance** test for pregnant women Rh(D) negative with partner Rh(D) positive

TURNAROUND TIME

3	5	K	**3-4** days
+	K+		**5-7** days
G	M	G+	**7-10** days

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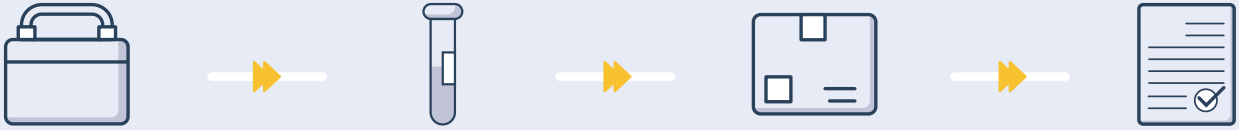
Maternal blood

Maternal blood + paternal buccal swab

4 EASY STEPS



Request the test kit

Collect the maternal blood sample

Ship the blood sample to Genomica Lab

Receive results

GENOMICA
Next Generation Genetics

ADVANCED MOLECULAR DIAGNOSTICS SOLUTIONS USING **STATE-OF-THE ART** TECHNOLOGIES

Over **100.000** genetic tests/year

Test performed in Italy
(Rome or Milan)

International **Partnerships**

20+ years experience in prenatal molecular diagnostics

Fast TAT **3 days**

Dedicated R&D team

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

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

LABORATORIES

Rome: Via Arduino 38 - 00162 - Tel.: +39 06.21115020
Milan: Viale L. Bodio 29-37 (Bodio 3) - 20158 - Tel.: +39 02.21115330
E-mail: info@genomicalab.it - **www.genomicalab.it**

REGISTERED OFFICE

Via Arduino 38 - 00162 Rome (RM)
info@pec.genomicalab.it
VAT and Fiscal Code: 14554101007 - REA: RM - 1530210

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