OMNIPT

Prenatal Cell-Free DNA Screening

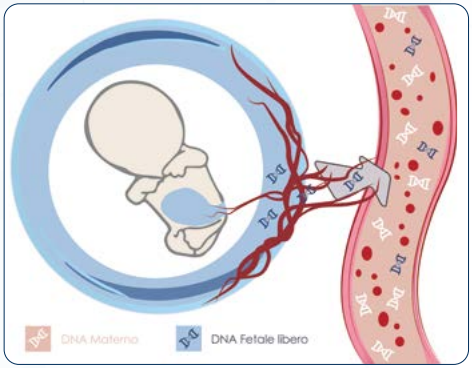
110 chromosome disorders with clinical interpretation

27 "*de novo*" monogenic disorders

BIOSCIENCE GENOMICS

Università di Roma Tor Vergata spin off

BIOSCIENCE GENOMICS is the University Spin-off of "Tor Vergata" Rome University and Bioscience Institute spa, in collaboration with BGI Europe.



FETAL CELL-FREE DNA

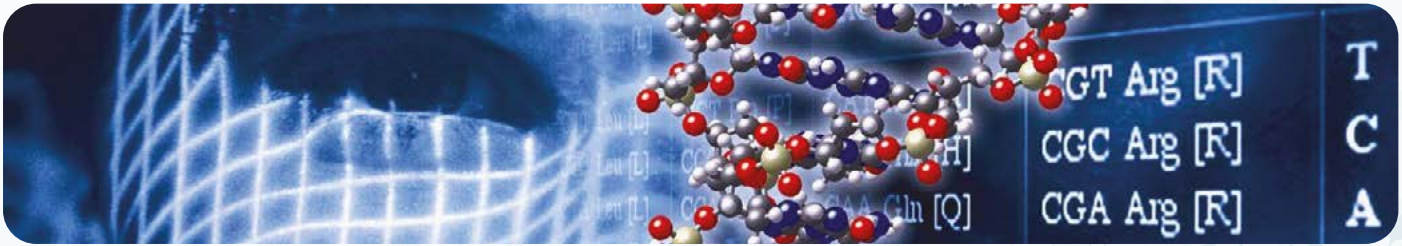
Maternal blood contains fetal cell-free DNA, which can be analyzed by whole-genome sequencing approaches based on the use of the new generation technologies (Massively Parallel Sequencing). This enables the early detection of genetic abnormalities that are associated with a large number of genetic syndromes.

THE TECHNOLOGY THAT DOES MAKE THE DIFFERENCE

"Targeted sequencing" exploited by some old-generation NIPT tests, as well as inexpensive approaches with non clinical validation don't allow for high-accuracy results. Thanks to whole-genome analysis and sophisticated bioinformatic analysis, OMNIPT methodology increases the accuracy of the obtained information, and extends the number of detectable conditions: trisomies, sex chromosome aneuploidies, deletion/duplication syndromes involving each chromosomes, and monogenic disorders.

EXPANDED PRENATAL SCREENING

OMNIPT is the expanded prenatal screening which enables the detection of 137 non-inherited genetic disorders, which are typically as unpredictable as serious. These disorders develops because of a mistake during germ cell production, a chromosome abnormality, or a genetic variant that occurs for the first time in the family ("*de novo*"). OMNIPT requires maternal peripheral blood, which is sampled when she is 10-24 weeks pregnant. Plasma DNA is extracted, sequenced, and analyzed by specific algorithms, in a few days.

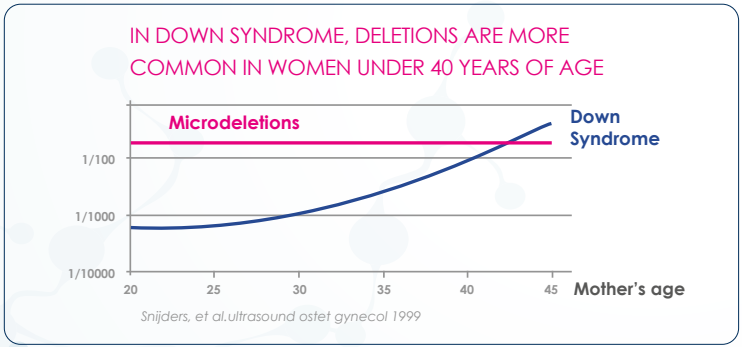


PRENATAL SCREENING AND CHROMOSOME DISORDERS

In chromosome disorders, there are extra chromosomes, or abnormalities in the structure of one or more chromosomes. For instance, Down syndrome is caused by one extra chromosome 21. The phenotype associated with these abnormalities depends on the involved chromosome, and on the size of the affected portion.

OMNIPT is the most complete and the most accurate cell-free DNA prenatal screening test analyzing chromosome disorders. Beside detecting **110 fetal chromosome abnormalities**, it provides a clinical interpretation of its results.

The analysis is based on the sequencing of millions of DNA fragments. The comparison with reference values enables an extremely accurate output. Even abnormalities consisting in microscopical defects in chromosome structure can be detected.



Condition	Sensitivity	Specificity	VPN
T21	99,17% [1]	99,95% [1]	>99,99% [1]
T18	98,24% [1]	99,95% [1]	>99,99% [1]
T13	>99,99% [1]	99,96% [1]	>99,99% [1]
Deletions Duplications	>90% [2]	ND	ND
Fetal sex	99,53% [3]	99,20% [3]	ND

Condition	Detection Rate	VPP	VPN
XYY	>99,9% [4]	50,00% [4]	>99,9% [4]
XXY	>99,9% [4]	42,86% [4]	>99,9% [4]
XXX	>99,9% [4]	70,00% [4]	>99,9% [4]
XO	>99,9% [4]	40,00% [4]	>99,9% [4]
RAA [5]	>99,9% [4]	ND	ND

1. Zhang et al., Non-Invasive Prenatal Testing For Trisomy 21, 18 and 13 - Clinical Experience from 146,958 Pregnancies. Journal of Ultrasound in Obstetrics and Gynecology, 2015
2. Internal analysis shows a sensitivity greater than 90% in the detection rate of deletion/duplication syndromes > 3Mb with fetal fraction ≥ 9,5%
3. Pan X, et al. Noninvasive fetal sex determination by maternal plasma sequencing and application X-linked disorder counseling. J.Matern Fetal Neonatal Med. 2014 Dec.
4. Jiang et al. Noninvasive Fetal Trisomy test: an advanced noninvasive prenatal diagnosis methodology for fetal autosomal and sex chromosomal aneuploidies. BMC Medical Genomics. 2012 5:57
5. Rare Autosomal Aneuploidies

OMNIPT: DETECTABLE CHROMOSOME DISORDERS

T21	Down syndrome
T18	Edwards syndrome
T13	Patau Syndrome

XO	Turner syndrome
XYY	Jacobs syndrome
XXX	Triple X syndrome
XXY	Klinefelter syndrome

–RAA*–

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

1p36 deletion syndrome
1p32-p31 deletion syndrome
1p31 deletion syndrome
1q41-q42 deletion syndrome
2p12-p11.2 deletion syndrome
2q31.1 duplication syndrome
2q33.1 deletion syndrome
2p16.1-p15 deletion syndrome
Holoprosencephaly 6
2q35 duplication syndrome
SHFM type 5
Dandy-Walker syndrome
3q13.31 deletion syndrome
3q29 duplication syndrome
3q29 deletion syndrome
3pter-p25 deletion syndrome
4q32.1-q32.2 triplication syndrome
Wolf-Hirschhorn syndrome
4q21 deletion syndrome
Cri du chat syndrome
5q12 deletion syndrome
5q14.3 deletion syndrome
6pter-p24 deletion syndrome
Chordoma
6q24-q25 deletion syndrome
6q11-q14 deletion syndrome
Monosomy 7q
7q11.23 deletion syndrome
7q11.23 duplication syndrome
8p23.1 deletion syndrome
8p23.1 duplication syndrome
8q22.1 duplication syndrome
8q22.1 deletion syndrome
Langer-Giedion syndrome
8q12.1-q21.2 deletion syndrome
Monosomy 9p
DiGeorge syndrome type 2
10q22.3-q23.2 deletion syndrome
10q26 deletion syndrome
Potocki-Shaffer syndrome
WAGR syndrome
Jacobsen syndrome
WAGRO syndrome
12q14 microdeletion syndrome
13q14 deletion syndrome
Frias syndrome
14q11-q22 deletion syndrome
Levy-Shanske syndrome
Distal monosomy 15q
Prader-Willi syndrome
Angelman syndrome
Congenital diaphragmatic hernia
15q14 deletion syndrome
15q11-q13 duplication syndrome
15q25 deletion syndrome
16q22 deletion syndrome
16p deletion syndrome
16p13.3 deletion syndrome
16p12.2-p11.2 deletion syndrome
16p11.2-p12.2 microduplication syndrome
17p13.3 duplication syndrome
17p13.3 deletion syndrome
Potocki-Lupski syndrome
Smith-Magenis syndrome
17q23.1-q23.2 deletion syndrome
17q21.31 duplication syndrome
17q12 duplication syndrome
17q12 deletion syndrome
Yuan-Harel-Lupski syndrome
De Grouchy syndrome
Monosomy 18q
19q13.11 deletion syndrome
Holoprosencephaly 1
DiGeorge syndrome
22q11.2 duplication syndrome
22q11.2 deletion syndrome
Cat eye syndrome
Xp11.3 deletion syndrome
Xq22.3 telomeric deletion syndrome
Xq28 deletion syndrome
Xp11.23-p11.22 duplication syndrome
Xp21 deletion syndrome
Xq27.3-q28 duplication syndrome
Xq21 deletion syndrome

* Rare autosomal aneuploidies

MONOGENIC DISORDER PRENATAL SCREENING

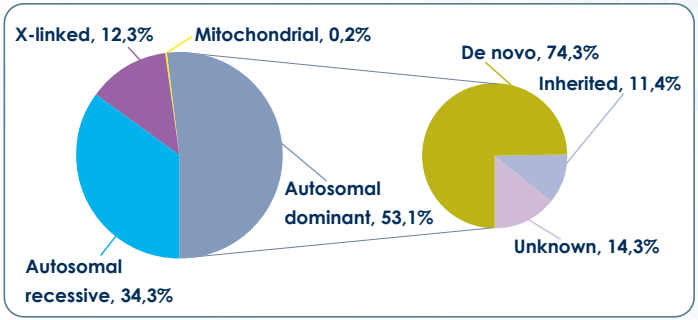
"*De novo*" autosomal dominant monogenic disorders are caused by mutations in a single gene and occur for the first time in a family. They are characterized by early onset. When present, these mutations are always manifested (complete penetrance).

The incidence of such disorders is 1/1,500. They correspond to 53% ca. of all of the diseases caused by a single gene mutation. In 74% of cases in which a monogenic disorder is not diagnosed, there is a "*de novo*" mutation.

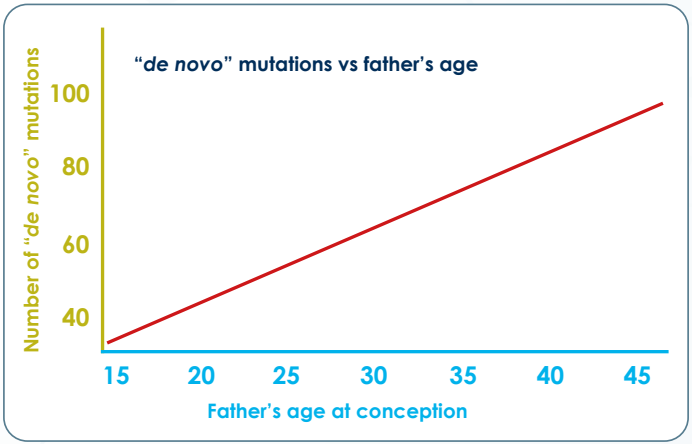
Missed diagnosis is linked both to the absence of the disorder in the parents, whose risk is not higher than the general population, and to the lack of early screening tools for such disorders. Ultrasounds can detect some alterations, but only later in pregnancy.

In the majority of cases, the phenotype is serious, and the prognosis is bad, because there are no drugs or other efficient treatments.

OMNIPT can detect up to 27 "*de novo*" autosomal dominant monogenic diseases in 18 genes, with a sensibility and a sensitivity greater than 99%.



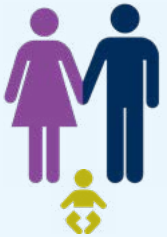
Yang, Y. et al. Molecular Findings Among Patients Referred for Clinical Whole-Exome Sequencing[J]. JAMA, 2014, 312(18):1870-1879.



It was demonstrated that the incidence of "*de novo*" mutation increases when parents' age (in particular father's age) increases.

- Kong A , Frigge M L , Masson G , et al. Rate of de novo mutations, father's age, and disease risk[J]. Nature, 2012, 488(7412):471-475.
- https://www.ncbi.nlm.nih.gov/books/NBK1116/

OMNIPT: DETECTABLE "DE NOVO" MONOGENIC DISORDERS



De novo

A single mother's or father's germ cell carries a mutation, which is transmitted to the son/daughter.
Otherwise, a mutation occurs in the zygote (fertilized egg) during the very first cell divisions.

GENE	MALATTIE SCHELETRICHE
COL1A1	Osteogenesis imperfecta type 1 Osteogenesis imperfecta type 2 Osteogenesis imperfecta type 3 Osteogenesis imperfecta type 4
COL1A2	Osteogenesis imperfecta type 1 Osteogenesis imperfecta type 2 Osteogenesis imperfecta type 3 Osteogenesis imperfecta type 4
FGFR3	Achondroplasia Thanatophoric dysplasia type 1 Thanatophoric dysplasia type 2 Crouzon syndrome with *acanthosis nigricans*
SOX9	Displasia campomelica Displasia campomelica acampomelica Displasia campomelica con inversione sessuale

GENE	SYNDROMIC DISEASE
BRAF	Cardio-facial-cutaneous syndrome 1
KRAS	Cardio-facial-cutaneous syndrome 2
MAP2K1	Cardio-facial-cutaneous syndrome 3
MAP2K2	Cardio-facial-cutaneous syndrome 4
HRAS	Costello syndrome
CHD7	Charge syndrome
TSC1	Tuberous sclerosis type 1
TSC2	Tuberous sclerosis type 2
COL2A1	Stickler syndrome type 1
COL11A1	Stickler syndrome type 2
STAT3	Hyperimmunoglobulin E syndrome
LMNA	Hutchinson-Gilford syndrome

GENE	CRANIOSYNOSTOSIS
FGFR1	Pfeiffer syndrome
FGFR2	Crouzon syndrome Apert syndrome Jackson-Weiss syndrome Pfeiffer syndrome

INDICATIONS*

- All the singleton pregnancy (also from homologous assisted reproduction)

ADVANTAGES

- Based on a simple mother's blood draw
- Suitable in the 10th to 24th pregnancy week
- 110 chromosome disorders detected, with clinical interpretation
- 27 monogenic disorders detected, with clinical interpretation
- Compensation in case of undetected disorders**
- Cost reimbursement** in case of diagnostic in-depth and/or genetic counseling

RELIABILITY

- The only test in the world enabling the detection of 110 chromosome and 27 monogenic disorders with clinical interpretation
- The most validated trisomy fetal cell-free DNA screening, with a clinical study involving 146,958 women
- More than 5 million tests been performed worldwide
- Sensitivity greater than 99% for trisomy 21, 18, and 13
- Sensitivity greater than 90% for deletions and duplications (submicroscopic too, until 3Mb)
- Sensitivity and specificity greater than 99% for monogenic disorders

*Before undergoing the test, carefully check with a qualified professional method's exclusion criteria.

**Insurance policy, compensations, and reimbursements are subject to limitations. For more information, please contact us before undergoing the test.

VALIDATION STUDIES AND BIBLIOGRAPHY

1. Zhang H, et al. Non-invasive prenatal testing for trisomies 21, 18 and 13: clinical experience from 146.958 pregnancies. Ultrasound Obstet Gynecol.2015 Jan 19.
2. Chen S, et al. A method for noninvasive detection of large fetal deletions/duplications by low coverage massively parallel sequencing. Prenat Diagn. 2013.
3. Liu et al. Performance evaluation of NIPT in detection of chromosomal copy number variants using low coverage whole genome sequencing of plasma DNA. Plos One, 2016.
4. Pan X, et al. Noninvasive fetal sex determination by maternal plasma sequencing and application X-linked disorder counseling. J.Matern Fetal Neonatal Med. 2014 Dec.
5. Jiang et al. Noninvasive fetal Trisomy test: an advanced noninvasive prenatal diagnosis methodology for fetal and sex chromosomal aneuploidies. BMC Medical Genomics, 2012.
6. Yang, Y. et al. Molecular Findings Among Patients Referred for Clinical Whole-Exome Sequencing[J]. JAMA, 2014, 312(18):1870-1879
7. Kong A , Frigge M L , Masson G , et al. Rate of de novo mutations, father's age, and disease risk[J]. Nature, 2012, 488(7412):471-475.
8. https://www.ncbi.nlm.nih.gov/books/NBK1116/

UNI EN ISO 9001:2015
CERTIFIED

BIOSCIENCE
GENOMICS

Numero Verde
800 690 914

www.bioinst.com - info@bioinst.com

ROMA
Università di Roma Tor Vergata
Via Ricerca Scientifica, 1 Roma

MILANO
Ospedale San Raffaele DIBIT 1
Via Olgettina, 58 Milano

Disclaimer

Features and conditions of described services are for illustrative purposes only and are subject to change

01 - 09 - 2020

BP - OM - REV0