Embryosafe®

eurofins | Genoma

The most limiting factor in ART is implantation failure, **responsible for over 72% of all failures**.
Chromosomal abnormalities are key causes of embryo implantation failure and early miscarriage.

WHAT **SOLUTION**?

		Recommended for		Advantages
 PGT-M	To detect in the embryo genome the presence of mutations related with the onset of **monogenic diseases**	• Partners carrying recessive mutations on the same gene (eg. Cystic Fibrosis) • Partner carrying an X-linked disorder (eg. Duchenne Muscular Dystrophy) • Partner suffering from autosomal dominant disease (eg. Huntington's disease)	• Partner carrying mutation predisposing to tumor development (eg BRCA1 and BRCA2) • Couple with a child or a previous pregnancy suffering from a monogenic disease • Couple wishing to perform the HLA matching test on the embryo	To reduce the risk of implanting an embryo with genetic anomalies inherited from the parents
 PGT-SR	To detect in the embryo genome the presence of **structural chromosomal rearrangements**	**One of the partner is aware of being a carrier of:**	• Inversions • Reciprocal translocations • Robertsonian translocations	To reduce the risk of transferring an embryo with structural chromosomal aberrations
 PGT-A	To detect in the embryo genome aneuploidies related **to reproductive failure and chromosomal disorders**	**All IVF patients and especially for:**	• Advanced maternal age (>35 years) • Recurrent miscarriages (two or more) • IVF failures (two or more) • Sperm defects	To reduce the risk of implanting an embryo with aneuploidies
 niPGT-A	To detect in the embryo genome aneuploidies related to reproductive failure and chromosomal disorders	**All IVF patients and especially for:**	• Advanced maternal age (>35 years) • Recurrent miscarriages (two or more) • IVF failures (two or more) • Sperm defects	To reduce the risk of implanting an aneuploid embryo and avoid embryo biopsy

Embryosafe® PGT-M

One or both partners in a couple may be unaware healthy carriers of genetic mutations responsible for **serious diseases that can be transmitted to their children**.

PGT-M is a genetic test for the **diagnose of MONOGENIC DISEASES** in the embryo allowing to transfer only unaffected embryos.

PGT-M test are customized to the couple's needs leading to the development of a **personalized diagnostic strategy** optimized for the specific genetic disease of which the couple is a carrier.

OUR **TECHNIQUES**

Minisequencing	**Fluorescent PCR**	**Linkage Analysis**
Point mutations	Small deletions/insertions	Complex mutations

PGT-M supports parents with children suffering from diseases, like leukemia, that can be treated **with hematopoietic stem cells**. It often happens that donors compatible with the patient are not available within the family. With the selective transfer it is possible to select embryos that are HLA compatible, allowing the **transplant of stem** cells harvested, for example, from the cord blood.

LIST OF MONOGENIC DISEASES DETECTED BY PGT-M

A

Achondrodysplasia
Acute necrotizing encephalopathy
Adrenogenital syndrome
Aggregated Tubular Myopathy 1
Aicardi-Goutieres syndrome
Aicardi-Goutieres syndrome 2
Alagille syndrome
Alpha 1 antitrypsin deficiency
Alport syndrome
Andersen syndrome
Androgen insensitivity
Aniridia

B

Bardet Biedl syndrome
Bardet-Biedel syndrome
Barth's syndrome
Beta thalassemia
Bifunctional protein deficiency
Breast and ovarian cancer, familial 1
Breast-ovarian cancer, familial 2
Brugada syndrome

C

Catecholergic polymorphic ventricular tachycardia
Central nucleus disease
Centronuclear myopathy
Charcot Marie Tooth 2A
Charcot Marie Tooth Type 2E
Charcot Marie Tooth X-linked
Charcot-Marie-Tooth 1A
Choroideremia
Cleidocranial Dysplasia, CCD
Combined oxidative phosphorylation defect 12
Combined oxidative phosphorylation defect, type 21
Congenital defect of glycosylation type Id
Convulsive syndrome 1
CPS1 deficiency
Craniosynostosis 1
Creutzledt-Jakob
Crisponi syndrome
CRMCC1
Crouzon syndrome
Currarino syndrome
Cystic fibrosis
Cystinosis, CTNS

D

Darier White's disease
Diamond Blackfan 3 anemia
DOORS syndrome
Duchenne muscular dystrophy

E

ECHS1D
EEC syndrome
Emery Dreifuss muscular dystrophy
Epidermolysis Bullosa

F

Fabry's disease
Facioscapulohumeral dystrophy
Familial adenomatous polyposis
Familial dysautonomia
Fanconi's anemia
Fetal myopathy
FISH eye disease
Fragile-X syndrome
Fraser syndrome
Freeman Sheldon syndrome
Friederich's ataxia
Epidermolytic hyperkeratosis

LIST OF MONOGENIC DISEASES DETECTED BY PGT-M

G

Gastric cancer
Gaucher syndrome
Gitelman Syndrome
GLB1 gangliosidosis
Gracil bone dysplasia
Gusher syndrome

H

Harlequin ichthyosis
Hemochromatosis
Hemolytic-uremic syndrome
Hemophilia A
Hereditary cerebellar cavernous malformation 2
Hereditary congenital myopathy
Hereditary deafness
Hereditary hydrocephalus
Hereditary sensorimotor neuropathy
Hereditary Spastic Paraparesis
Hereditary spastic paraparesis 10 SPG10
HLA matching
Huntigton's disease
Hypertrophic cardiomyopathy
Hypertrophic cardiomyopathy
Hypohidrotic ectodermal dysplasia

I

Incontinentia Pigmenti
Infantile encephalopathy
Infantile epileptic encephalopathy
Infantile hypophosphatasia
Isolated complex III deficiency

J

Joubert syndrome

K

KGB syndrome
Krabbe's disease

L

Leri Weill Syndrome
Lethal restrictive dermopathy
Leukoencephalopathy syndrome - LTBL
LGMD1F cingulate muscular dystrophy
Li-Fraumeni syndrome
Loken syndrome type 5
Long QT syndrome
Lynch syndrome

M

Marfan syndrome
Mature onset juvenile diabetes type 3
Meckel Gruber Syndrome
Mental retardation
Metachromatic leukodystrophy
Metaphyseal chondrodysplasia
Methylmalonic acidemia
MGCA7
Microdeletion
Microdeletion
Microduplication
Mitochondrial DNA depletion syndrome
MODY 3
Mucopolysaccharidosis type 2
Multiple endocrine neoplasia type 2A
Multiple Epiphyseal Dysplasia Type 4
Multiple exostosis type 1
Multiple exostosis type 2
Multiple Synostoses Syndrome 1
Myoclonic dystonia
Myofibrillar myopathy 3
Myotonic dystrophy 2
Myotonic dystrophy type 1

LIST OF MONOGENIC DISEASES DETECTED BY PGT-M

N

Nail Patella syndrome
Narcolepsy
Netherton syndrome
Neurofibromatosis type 1
Neurofibromatosis type 2
Niemann-pick C2 disease
Nonketotic hyperglycemia
Non-syndromic sensory deafness
Noonan syndrome
Norrie's disease

O

Occult macular dystrophy
Ocular albinism type 1; OA1
Okihiro syndrome
Osteogenesis Imperfecta Type1
Otosponsilomegaepiphyseal dysplasia

P

Pachyonychia Congenita
Paramyotonia Congenita
Periventricular nodular heterotropy
Peutz-Jeghers Syndrome
Polycystic kidney disease
Polycystic kidney disease 4
Polycystic kidney type 1
Polycystic kidney type 2
Primary dystonia
PROMM
Propionic aciduria
Pseudoachondroplasia
PVHH

R

Renal cysts and diabetes syndrome
Retinitis Pigmentosa
Retinitis Pigmentosa 2
Retinoblastoma
Retinoschisis
Rett Syndrome
Rh alloimmunization
RIEG3

S

Saethre-Chotzen syndrome
Sandhoff disease
Schimke's Syndrome
Semialdehyde succinic dehydrogenase deficiency
Severe combined immunodeficiency
Shwachman-Diamond syndrome
Spastic paraplegia - 2
Spastic paraplegia 5A
Spinal muscular atrophy
Spinocerebellar ataxia 6
Spinocerebellar ataxia type 1
Spinocerebellar ataxia type 14
Spinocerebellar ataxia type 2
Spinocerebellar ataxia type 2
Stargardt's disease
Stickler's syndrome
Stuve Wiedeman
SVAS
Syndromic secondary plateletopenia
SYNS1

LIST OF MONOGENIC DISEASES DETECTED BY PGT-M

T

TAR syndrome
Telangiectasia
TP53 mutation
Treacher Col syndrome
Trichohepatoenteric syndrome
Trifunctional protein deficiency
Tuberous sclerosis
Tuberous sclerosis type 2
Type 1 optic atrophy

U

UPD14
Usher syndrome
Usher syndrome

V

Van der Woude syndrome
Von Hippel-Lindau syndrome

W

Wolcott Rallison syndrome

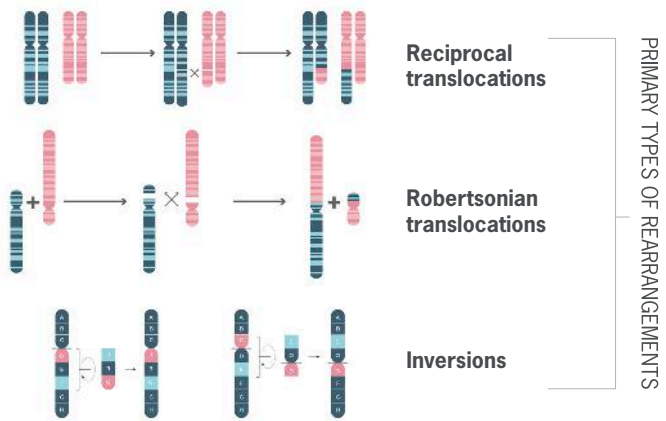
X

X-linked ichthyosis
X-linked MED12 disease
X-linked mental retardation
X-linked ornithine
X-linked syndromic mental retardation

Z

Zellweger syndrome

Embryosafe®
PGT-SR



It has long been known that chromosomal rearrangements have a significant impact on fertility and miscarriage risk.

Couples with chromosomal structural rearrangements undergoing natural conception have a risk (**50% or more**) of chromosomal abnormalities, which can increase the miscarriage rate and decrease the live birth rate.

PGT–SR is a genetic test able to identify unbalanced chromosomal rearrangements in the embryo prior to its transfer, increasing the chances of reaching a pregnancy of having a successful pregnancy.

OUR TECHNIQUE

NGS
(Next Generation Sequencing)

- No set-up required.
- Detection of segmental abnormalities up to 5Mb.
- Possibility of screening all 24 chromosomes together with chromosomal rearrangements (PGT-SR + PGT-A).

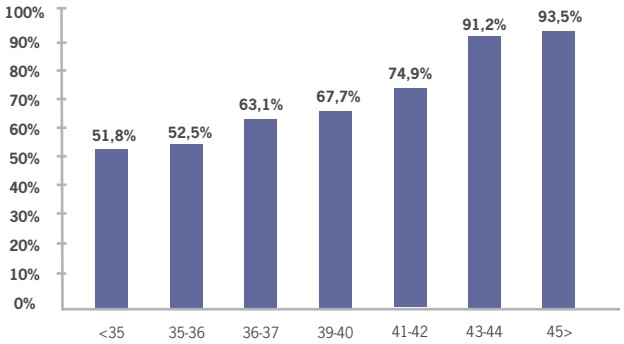
Embryosafe®
PGT-A

Every couple is at risk of conceiving chromosomally abnormal embryos, and maternal age (>35 years) increases this risk.

It is believed that, in most cases, aneuploidy causes embryos to either fail to implant after transfer or spontaneously abort early in gestation.

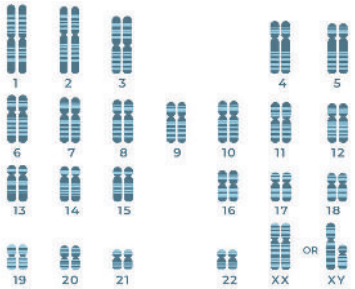
PGT-A allows to identify euploid blastocysts and increase the chance of **reproductive success during IVF**.

% aneuploidy in embryos increases with maternal age

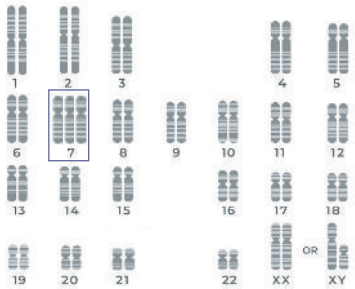


Data from 8000 blastocysts by NGS

EUPLOID KARYOTYPE



ANEUPLOID KARYOTYPE



The anomaly found is incompatible with life

Embryosafe® PGT-A

PGT-A RESULTS

EMBRYO CHROMOSOMAL CONTENT	Euploid 	Aneuploid 	Mosaic* 
CHROMOSOMAL CONTENT PER CELL	**Normal**	**Abnormal**	**Mixed** (Some normal and some abnormal cells)
LIKELIHOOD OF ACHIEVING A SUCCESSFUL PREGNANCY	**High**	**Very unlikely**	**Lower than euploid embryos** but possible
RECOMMENDED FOR TRANSFER	**Yes**	**No**	**May be considered if no euploid embryos are available for transfer** only after a proper genetic counselling

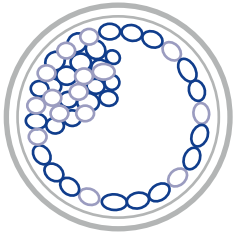
* Greco E, Minasi MG, Fiorentino F. Healthy babies born after intrauterine transfer of mosaic aneuploidy, blastocyst. N Engl J Med 2015; 373:2089-2090

Spinella F, Fiorentino F, Biricik A, et al. The extent of chromosomal mosaicism influences the clinical outcome of in vitro fertilization treatments. Fertil Steril 2018;109:77-83.

Embryosafe® PGT-A

FOCUS ON MOSAICISM

Mosaic embryos are embryos in which there are cell populations with different chromosomal contents. In mosaic embryos, the simultaneous presence of both euploid and aneuploid cells is detected.



EUPLOID CELL
ANEUPLOID CELL

Mosaicism results from errors in mitosis during the embryonic development. The timing of these errors, with respect to the stages of cell replication, determines how **many cells will be affected**. In any case, such errors are independent of maternal age.

Thanks to NGS it is possible to identify mosaic embryos.

LOW-LEVEL MOSAICS

- Aneuploidy rate **<50%**
- High priority when there aren't euploid embryos available

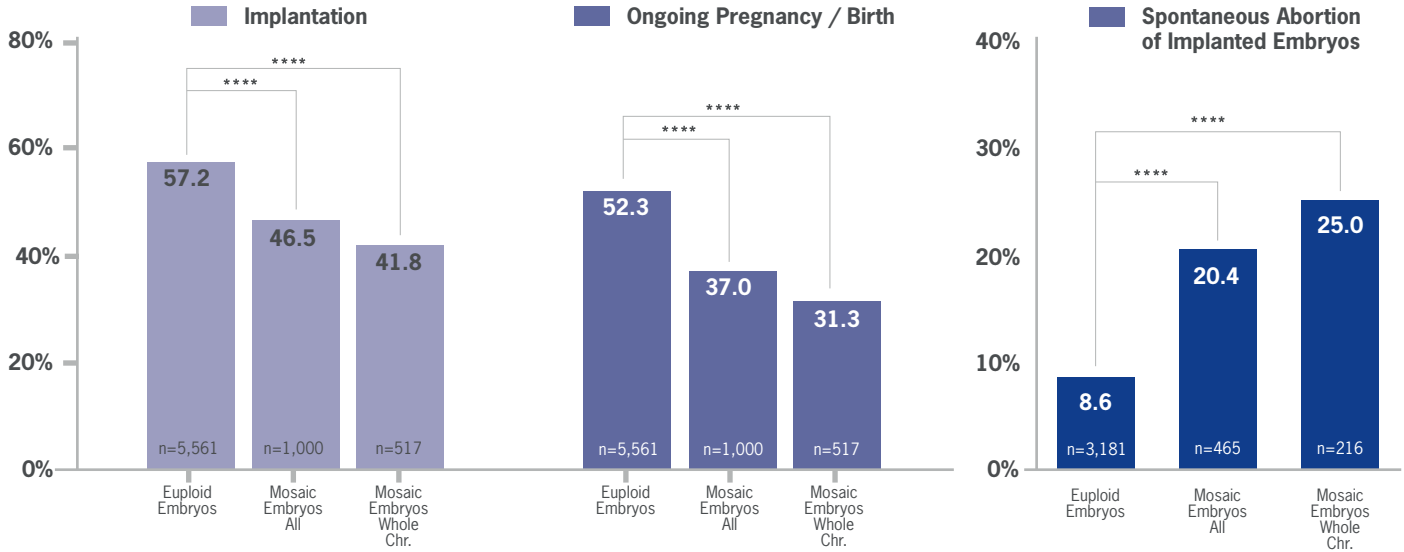
HIGH LEVEL MOSAIC

- Aneuploidy rate between **≥50%**
- Low priority when there aren't euploid embryos available

COMPLEX MOSAICS

- Mosaicism detected in **3 or more chromosomes**
- Lowest priority when there aren't euploid embryos available

Spinella F, Fiorentino F, Biricik A, Bono S, Ruberti A, Cotroneo E, Baldi M, Cursio E, Minasi MG, Greco E. Extent of chromosomal mosaicism influences the clinical outcome of in vitro fertilization treatments. Fertil Steril. 2018 Jan;109(1):77-83. doi: 10.1016/j.fertnstert.2017.09.025. Epub 2017 Nov 28. PMID: 29191449.



- ✓ **PGT-A** can represent a valid support to the clinic for embryo selection in case of mosaicism.
- ✓ **Via PGT-A** is possible to detect and characterize mosaicisms that affect implantation and spontaneous abortion.
- ✓ **Eurofins Genoma**, as part of an international multi-center study, has actively collaborated in the creation of an embryo ranking combining mosaic level, type, and embryo morphology. This ranking system can make it easier for the clinic to choose the best embryo to transfer.

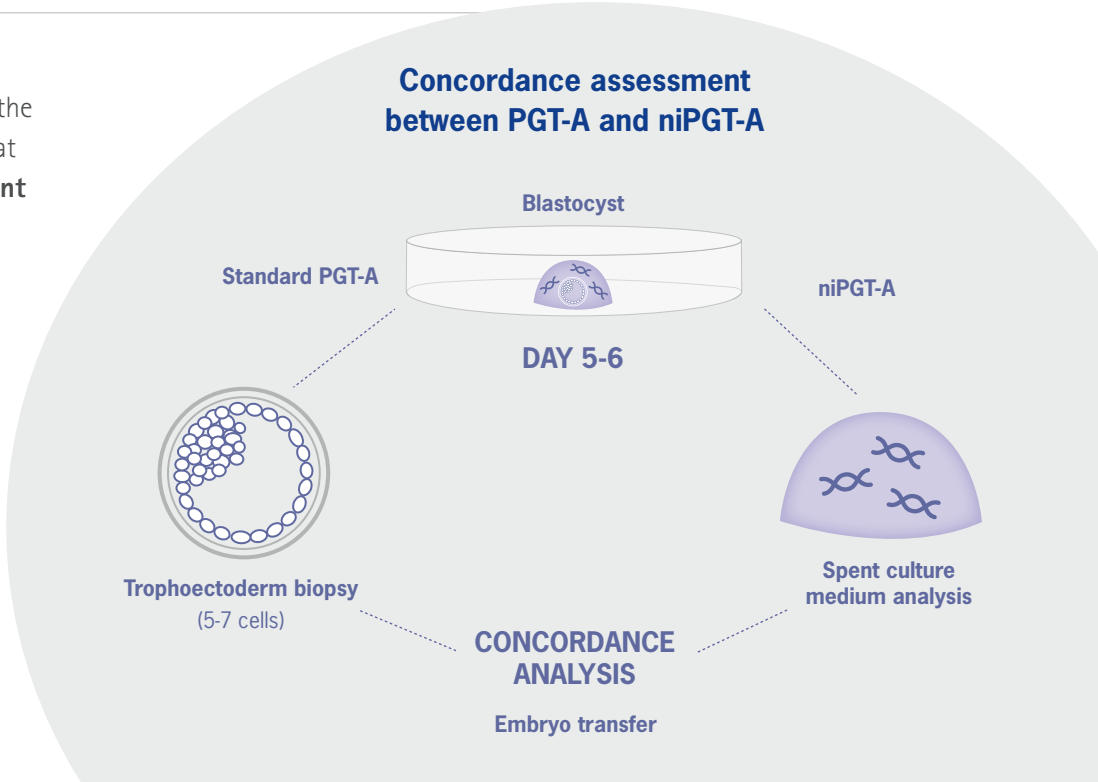
Viotti M, Victor AR, Barnes FL, Zouves CG, Besser AG, Grifo JA, Cheng EH, Lee MS, Horcajadas JA, Corti L, Fiorentino F, Spinella F, Minasi MG, Greco E, Munné S.
Using outcome data from one thousand mosaic embryo transfers to formulate an embryo ranking system for clinical use. Fertil Steril. 2021

Embryosafe®
niPGT-A

The **Non Invasive PGT-A (niPGT-A)** is an innovative procedure that **allows to detect aneuploidies** without manipulating the embryo.

This test is based on the analysis of the **embryo cell free DNA (cfDNA)** that can be easily collected from the **Spent Culture Media (SCM)** in which the blastocyst is placed.

The use of the cfDNA avoids the need to biopsy the embryo for the collection of cells from the trophoectoderm.



Concordance assessment, study results

OUR EXPERIENCE

	D3-D5	D3-D6	D4-D6
No. of samples analyzed	154	180	121
No. of samples with positive WGA amplification	147/154 **(95,5%)**	179/180 **(99,4%)**	119/121 **(98,3%)**
No. of samples with an informative result	95/147 **(64,6%)**	145/179 **(81,0%)**	102/119 **(85,7%)**
No. of samples with PLOIDY concordance	69/95 **(72,6%)**	123/145 **(84,8%)**	90/102 **(88,2%)**
No. of samples concordant for ALL CHROMOSOMES	39/69 **(56,5%)**	69/123 **(56,1%)**	52/90 **(57,8%)**
No. of samples concordant for OTHER CHROMOSOMES	30/69 **(43,5%)**	54/123 **(43,9%)**	38/90 **(42,2%)**
No. of discordant samples	26/95 **(27,4%)**	22/145 **(15,2%)**	12/102 **(11,8%)**
No. of false positive samples	16 **(16,8%)**	12 **(8,3%)**	7 **(6,8%)**
No. of false negative samples	10 **(10,5%)**	10 **(6,9%)**	5 **(4,9%)**
	Sentitivity: 83,61 **Specificity:** 52,94	**Sentitivity:** 90,91 **Specificity:** 65,71	**Sentitivity:** 93,67 **Specificity:** 69,57

Biricik et al., ESHRE 2022

Huge number of samples analyzed

Very high ploidy concordance

CELL FREE DNA ANALYSIS FOR AN EASIER PGT

ADVANTAGES

- ✓ Possibility of combining PGT-M, PGT-A and PGT-SR
- ✓ Genetic counselling
- ✓ High resolution testing (NGS Technology)
- ✓ Personalized set up
- ✓ Accuracy >99%
- ✓ HLA matching available
- ✓ Fast TAT: 24h for fresh transfer/7-10 days for frozen embryos

SHIPPING BOX

The box contains all necessary consumabels/reagents necessary for the transport of biopsied cell samples in maximum protected conditions.

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