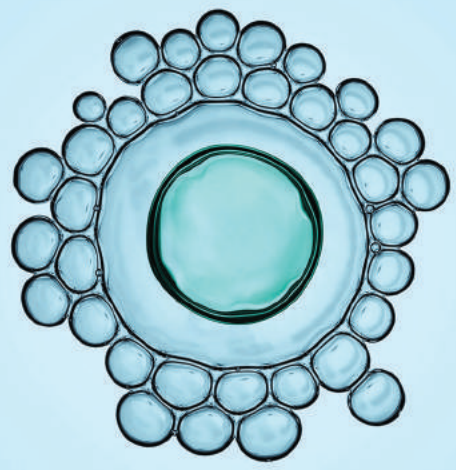
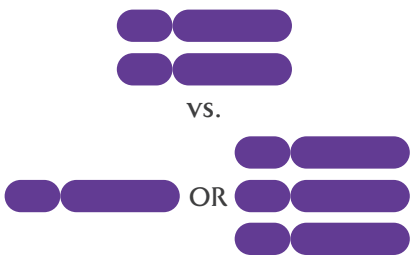
COMPREHENSIVE PREIMPLANTATION GENETIC TESTING

What Is Preimplantation Genetic Testing (PGT)?

PGT is the process of screening embryos produced during in-vitro fertilisation (IVF) for genetic diseases and chromosomal disorders before they are transferred to the woman's uterus. PGT, thus, gives accurate information about the embryo's health and helps you to choose the best embryo increasing the chances of a live birth.



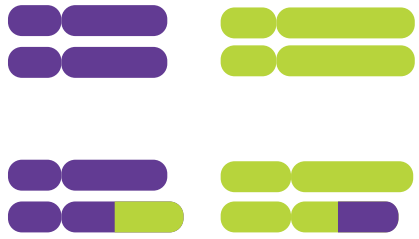
MFine diagnostics offers:



PGT-A

Preimplantation Genetic Testing - Aneuploidy (PGT-A) screen embryos for:

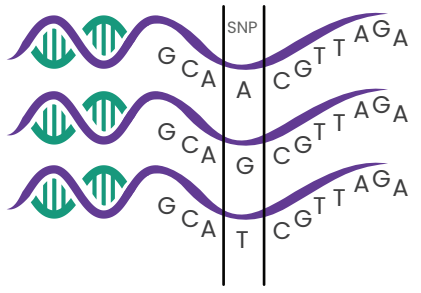
- Whole Chromosome Aneuploidy (WCA)
- Copy Number Variation (CNVs)
- Mosaicism



PGT-SR

Preimplantation Genetic Testing - Structural Rearrangement (PGT-SR) screen embryos for:

- Unbalanced Translocations
- Inversions
- Includes PGT-A



PGT-M

Preimplantation Genetic Testing - Monogenic defects (PGT - M) screen embryos for Inherited, Single Gene Disorders that are:

- Autosomal Recessive
- Autosomal Dominant
- X-Linked

Name of Salesperson: ..... Contact: .....

support@mfine.co www.mfine.co

How Does The PGT Process Work?

PGT-A requires embryo biopsy, the removal of either a single or a small number of cells from a growing embryo. The procedure can be performed on day 3 after egg retrieval, or more commonly, on days 5–7 when embryos reach the blastocyst stage of development.

For the reasons mentioned below, trophectoderm cell biopsy on Blastocyst Stage (day 5 or 6) is preferred (1):

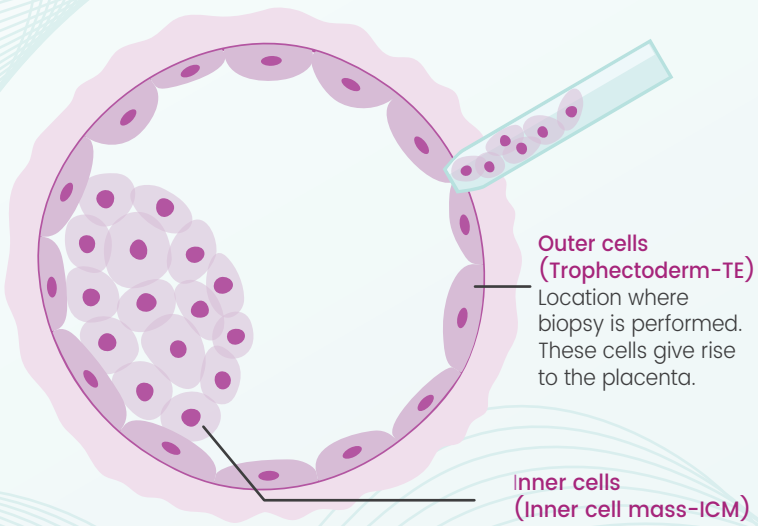
Blastomere Biopsy - Day 3

- Single Cell = Less DNA
- Poorer representation of embryo's genetic cells (1 cell only)
- Higher test failure rate as only one/two cell(s) is available for analysis
- Mosaicism cannot be detected
- Detrimental to the health of the embryo

Trophectoderm Biopsy - Day 5

- More cells (8-10 cells) = More DNA
- Better representation of embryo's genetic cells (few cells)
- Lower test failure rate as more number of cells are available for analysis
- Mosaicism can be detected
- Resilient to the embryo

Which is why MFine prefers a Trophectoderm Biopsy Sample



Blastocyst Terminology:
Outer Cell (Trophectoderm - TE)
Location where biopsy is performed.
These cells give rise to the placenta.

Inner cells (Inner cell mass - ICM)
Cluster of cells that give rise to the fetus.

The first step of PGT is to go through an IVF treatment cycle.

During the IVF cycle, each egg is fertilized with sperm.

The embryos are cultured for five or six days until they become blastocysts.

Those embryos that can grow to become good-quality blastocysts are biopsied whereby a few trophectoderm (TE) cells are removed from the blastocyst.

These cells are "extra-embryonic" and will produce tissues such as the placenta.

An ALL-Chromosome Preimplantation Genetic Testing for Aneuploidy (PGT-A)

For couples undergoing in-vitro fertilisation (IVF), PGT-A improves the chance of a healthy pregnancy by identifying embryos with extra or missing chromosomes, also called aneuploidy.

Embryos with the correct number of chromosomes (23 pairs) have the highest chance of successful implantation and the lowest chance of miscarriage.

How Does Aneuploidy Occur?

Most of the time, aneuploidy occurs by chance during the formation of an egg or sperm, or during the development of an embryo. Embryos with aneuploidy often fail to implant, and those that do implant often result in miscarriage.

A pregnancy with aneuploidy can sometimes lead to a live birth.

However, in most cases, these babies will have physical abnormalities and/or intellectual disabilities.

The most common aneuploidy in live-born babies is trisomy 21, also known as Down syndrome

Normal pairing (euploid)

One copy of each chromosome from egg and sperm

Normal embryo

Abnormal pairing (aneuploid)

More than one copy of chromosome from egg or sperm

Embryo with Trisomy

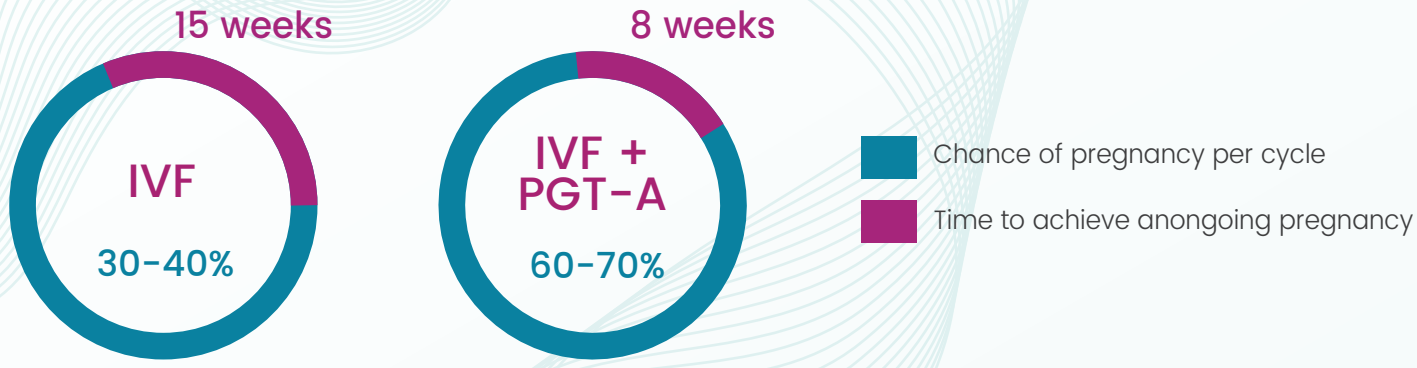
Missing one copy of a chromosome from egg or sperm

Embryo with Monosomy

Benefits Of Choosing PGT-A For IVF Couples

Ensures embryos have the correct number of chromosomes - a crucial factor in the success of pregnancy (2-5)

- Increases implantation success rates while decreasing the chance of miscarriage (8-11)
- Increases live birth rate
- Reduces time to pregnancy and extra cycle costs
- Increases the chance of the birth of a healthy baby
- Enables transfer of a single embryo with higher confidence instead of multiple embryos, reducing the likelihood of complications associated with multiple pregnancies (9,12)



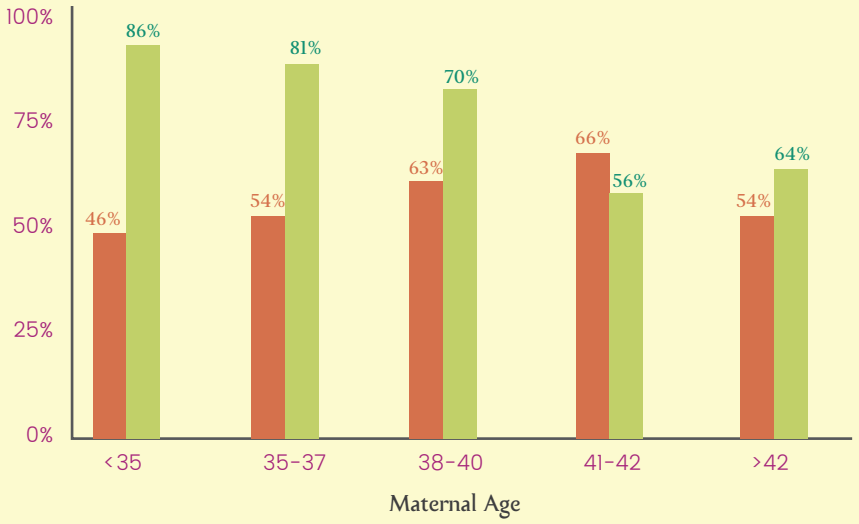
PGT-A doubles the chance of pregnancy per cycle and cuts the time to achieve an ongoing pregnancy to half [13-14]

Chance Of Having At Least One Euploid Tested Embryo Per IVF Cycle In PGT-A

The chance of aneuploidy in embryos increases with the mother's age[1]

However, for high maternal age groups also, with PGT-A there is a great chance of having at least one PGT-A normal embryo available for implantation[1]

PGT-A Analysis



Number of Embryos: 23,561

Number of fertility clinics: 57

Of all 4,833 IVF cycles evaluated,

3,675 (76%)

had at least one embryo with a normal PGT-A result

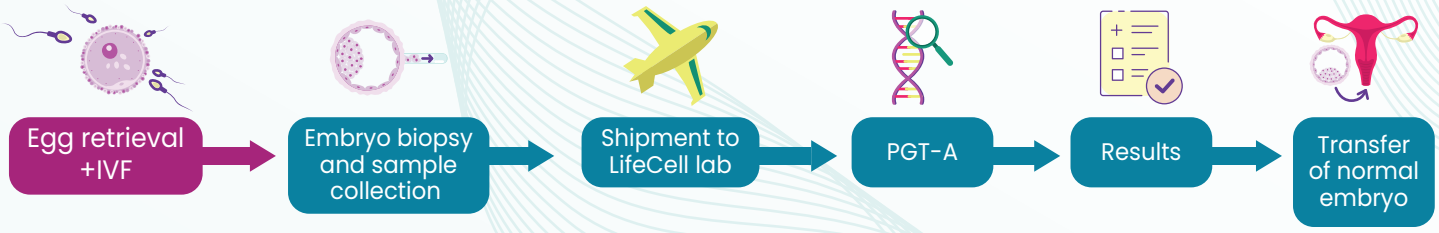
Who Is At A Higher Risk Of Aneuploidy?

While any couple can have an embryo with aneuploidy, the chances can increase with the following factors:

- Advanced maternal age - 35 or older.
- Women who suffered two or more miscarriages
- Women after two or more failed in vitro fertilisation cycles.
- Male factor - substantial alterations of sperm parameters may indicate the presence of an altered number of chromosomes in the sperm cells.
- Couples who experienced an altered number of chromosomes during a previous pregnancy.
- Couples who are carriers of numerical abnormalities in the sex chromosomes (X or Y).

The PGT-A Process

Preparation/Monitoring follicular development



Possible PGT-A Results:

	EUPLOID	MOSAIC	ANEUPLOID
Number of chromosomes per cell	Normal	Mixed (some normal & some abnormal)	Abnormal
Likelihood of producing a successful pregnancy	High	Low, but possible	Very unlikely
Transfer priority	High	Intermediate, may be considered if no euploid embryos are available	Low

Preimplantation genetic testing for chromosomal Structural Rearrangements -PGT-SR

Chromosomal rearrangements are changes from the normal size or arrangement of chromosomes, which are the structures that hold our genetic material.

It is estimated that 1 in every 500 people carry a balanced reciprocal translocation.

People who have a chromosome rearrangement are at risk of creating embryos with the incorrect chromosome number or structure.

This usually does not lead to a successful pregnancy or may result in the birth of a child with genetic abnormalities.

PGT-SR is a test to identify embryos with the correct amount of genetic material (balanced/normal) and embryos that have extra or missing genetic material as a result of the translocation or rearrangement (unbalanced).

PGT-SR reduces the chance of a failed implantation or miscarriage, or of having a child with a chromosomal abnormality, and increases the likelihood of a healthy pregnancy after an IVF cycle.

Who is PGT-SR for?

PGT-SR for chromosome rearrangements is useful for couples who had a child or pregnancy with a chromosome rearrangement or if one or both are a carrier of an:

Duplications:
A segment of the chromosome is repeated

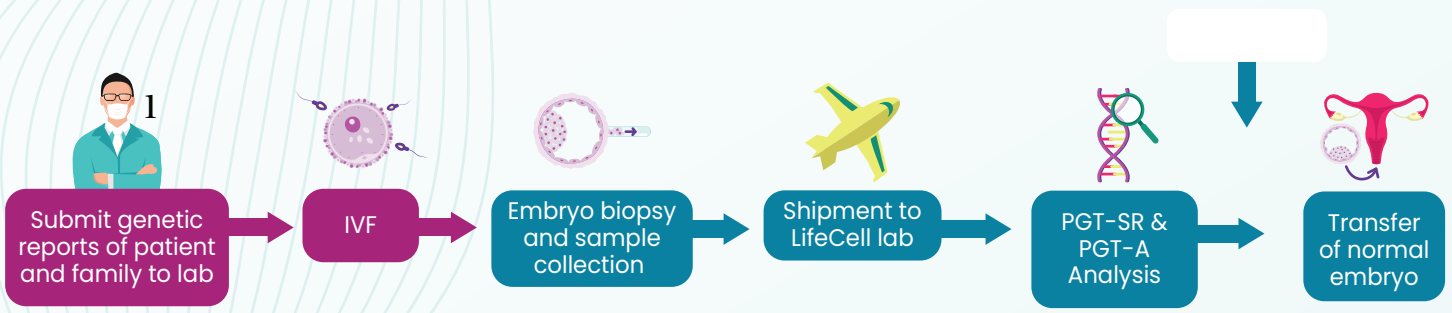
Deletions:
A segment of the chromosome is missing

Inversion:
A segment of chromosome reverses its orientation

Translocation:
A segment of the chromosome changes its location. Two different types of translocations are Reciprocal translocation and Robertsonian translocation

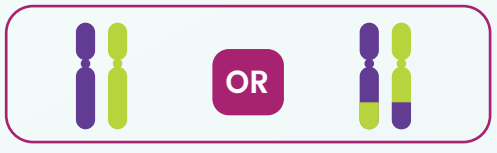
The PGT-SR Process

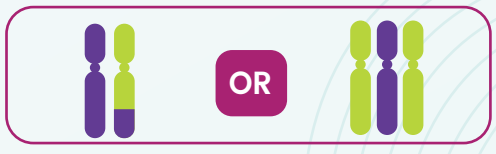
The Couple reports are reviewed by experts at LifeCell to determine if PGT-SR is appropriate. Embryo biopsy samples are then sent to our lab where testing is conducted. PGT-SR screens out embryos that carry unbalanced translocations, ensuring only those with the correct amount of genetic material are selected for transfer.



PGT-SR at mfine is automatically paired with the PGT-A result at no additional charges!

Possible PGT-SR Results:





Chromosome Status	Euploid or Balanced	Unbalanced/Aneuploid
Likelihood of producing successful pregnancy	High	Very Unlikely
Transfer priority	High	Low

A genetically normal or balanced embryo is chosen for transfer to the mother's uterus, which increases the chances of carrying and delivering a healthy baby.

The Superior Technology Benefit

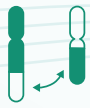
A Validated Solution for PGT-A and PGT-SR

MFine is committed to offering the most advanced PGT technology to enable the most informed embryo selection. A robustly validated PGT-A solution that has been favourably benchmarked against the other commercially available PGT-A kits

For PGT, Next Generation Sequencing (NGS) workflows offer improvements in accuracy, sensitivity and resolution over other platforms such as microarrays or FISH for the detection of aneuploidy and copy number variants (CNVs) in embryos. Our high-resolution PGT is performed via NGS technology for efficient, streamlined workflow to provide unparalleled detection of:

Aneuploidy

Partial (segmental) aneuploidy

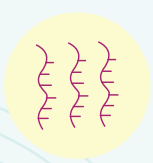


Unbalanced translocations

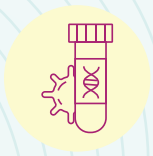
Mosaicism

Benefits of MFine PGT

Analyses picogram quantities of DNA
Employs a two-step approach of Whole Genome Amplification (WGA) followed by library preparation



Utilises a single tube from DNA to sequenced data
All reagents required for whole genome amplification and library preparation are added in the same biopsy tube



Reduces the risk of sample contamination
Requires only three tube openings

Superior Analysis Software
Automated calling of aneuploidy and copy number variants

Validation
Validated for known ploidy, including euploid, single, and double trisomies. Cell line aberrations (gains and losses) of 7-31 Mb.

Superior Specification
Utilises 1 x 75 bp read lengths, double the length offered by the other commercially available
PGT-A kits

Higher Resolution
This additional read length provides 15% more mapped reads per sample and 50% more coverage across the sequenced genome allowing lossless resolution and accuracy.

Increased yield
Degenerate Oligonucleotide Primed PCR (DOP-PCR)-based Whole Genome Amplification largely reduces the chances of amplification failure.

Fast
3 Hours sample preparation time

High throughout
96 samples can be analysed in one go

Quality Control
At every step - Whole Genome Amplification / Sequencing Analysis

Preimplantation Genetic Testing For Monogenic Disorders - PGT-M

Choose PGT-M to help families avoid passing down genetic conditions to the next generation!

A single gene condition is caused by a change, known as a mutation, in a particular gene which causes that gene to function improperly or not function at all. There are thousands of single-gene conditions that are passed through families.

Preimplantation genetic testing for monogenic/single gene defects (PGT-M) is a genetic test that analyses DNA from each embryo for the presence of a specific genetic mutation during an IVF treatment cycle. By avoiding the transfer of affected embryos, patients can be sure that children resulting from IVF are free from the disease.

Who Should Consider PGT-M?

PGT-M is invaluable to those at higher risk of transmitting a genetic disease to their children

The embryo is at an elevated risk of a genetic disorder due to one of the following:

- Both biological parents are known carriers for the same autosomal recessive disorder
- One biological parent is a known carrier of an autosomal dominant disorder
- One biological parent is a known carrier of an X-linked recessive disorder.
- Biological parents has/had a child affected by a genetic disease.

Which Disorders Can PGT-M Screen For?

PGT-M can be performed for >6000 single gene disorders, including

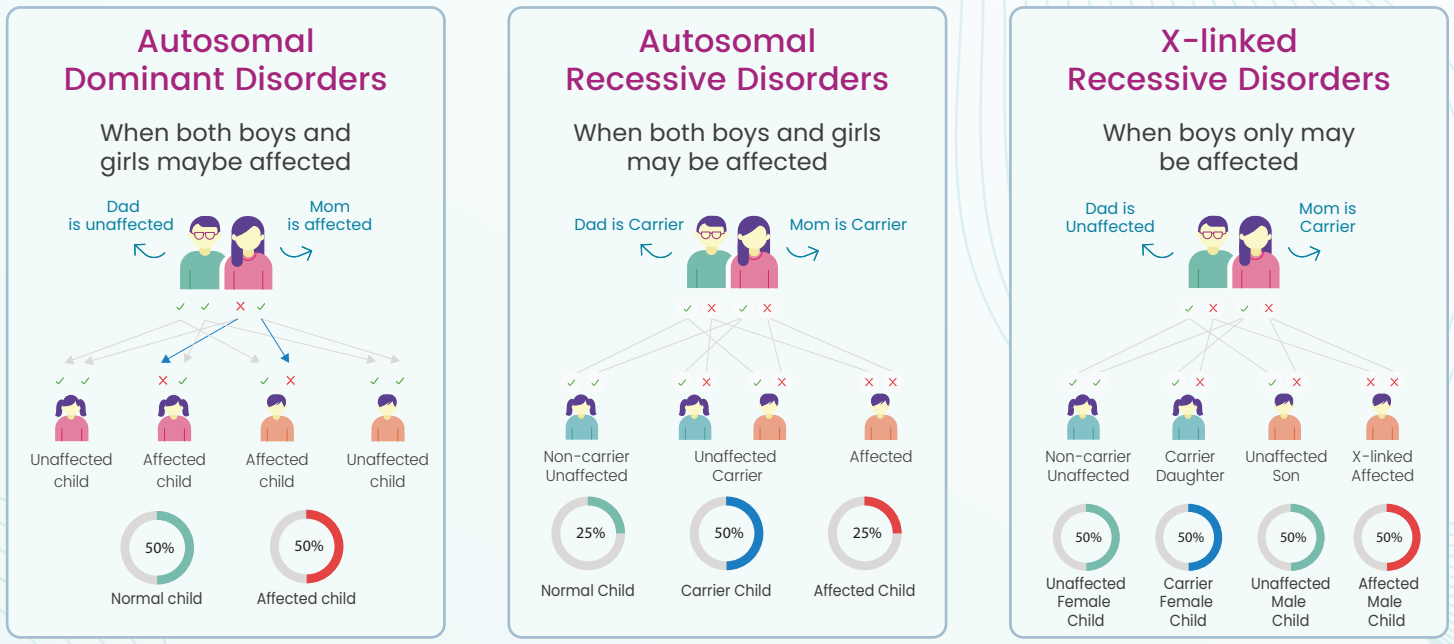
- Thalassaemia
- Duchenne Muscular Dystrophy
- Cystic Fibrosis
- Haemophilia
- Spinal Muscular Atrophy
- Hereditary cancer syndromes such as BRCA 1 and 2

How To Identify A Carrier?

Families learn about their risk status through an affected family member, child, or pregnancy, or as a result of carrier screening. Before planning a pregnancy it is essential to evaluate whether a couple is a carrier of genetic mutations that could be transmitted to their children.

MFine's GenePass Comprehensive is a 2000+ genes PAN-ETHENIC, EXPANDED, NGS-based Carrier Screening Test. It includes all the conditions recommended by ACMG and ACOG for universal carrier screening during pregnancy and preconception. DMD, SMA carrier screening is offered with MLPA technology and Fragile-X screening can be additionally included.

For identified carriers, what is the likelihood of having an affected child?
The likelihood of having an affected child depends on the type of genetic condition carried



Autosomal Dominant Conditions: One of the parents carries the affected gene and suffers from the disease. 50% of their offspring will be unaffected and 50% will inherit the mutated gene and therefore suffer from the disease.

Autosomal Recessive Conditions: Having just one of the affected copies of the gene translates into being a carrier that does not affect their health but puts their children at risk of inheriting the genetic condition. The disease is manifested, when both the maternal and the paternal copies have the mutated gene. In this case, 25% of the offspring will be unaffected, 50% will become unaffected carriers and 25% will be affected by the disease.

X-Linked Conditions: A female carrying a mutation in one gene, with a normal gene on the other X chromosome, is generally unaffected but translates into a carrier. The disease is manifested in male offspring when the X chromosome has the mutated gene. 50% of their male offspring will be affected and 50% of their female offspring will be carriers.

How Does PGT-M Work?

Unlike blood sample testing, PGT-M uses a special genetic testing technique to pick up the mutation accurately from the few-cell biopsy sample. With the knowledge of the disease, the inheritance, family history and the exact mutation, we create a custom-designed test which is unique to each family.

Step 1 : Clinician Referral And Review The Clinician submits genetic testing reports for case review and approval. The family's genetic reports and history is assessed. The lab may require Genetic testing reports of additional family members. Post review lab confirms if this case can be taken up for PGT-M.

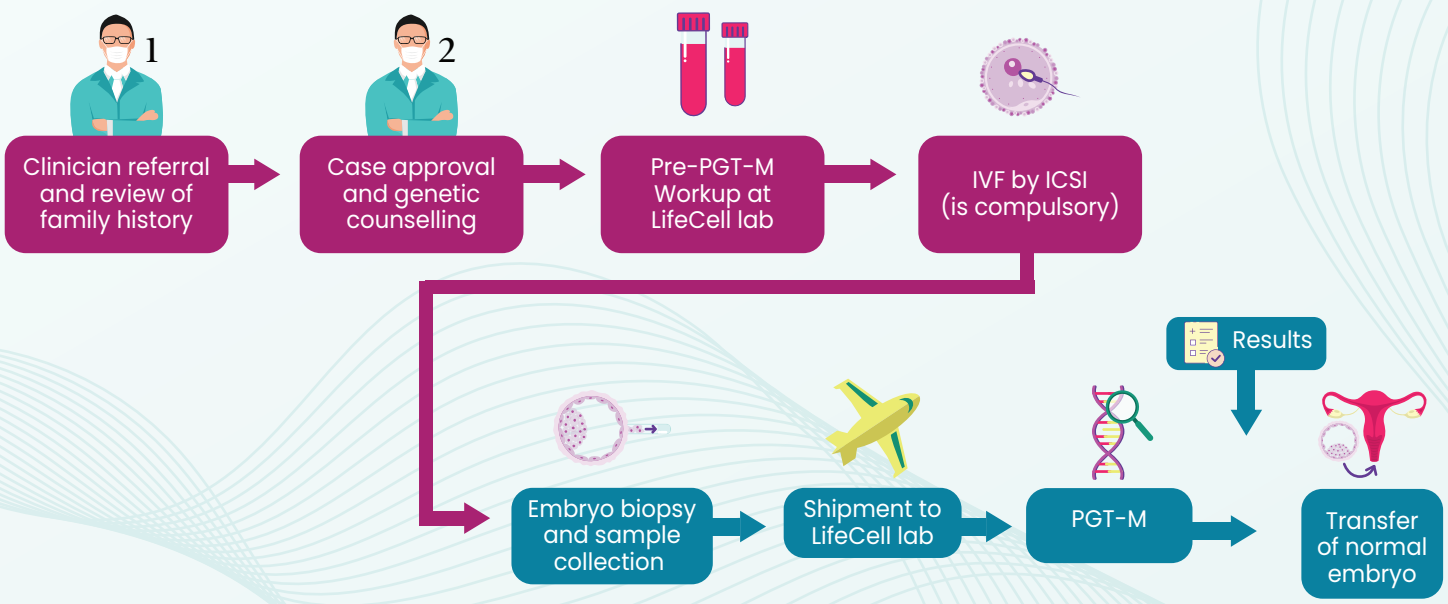
Step 2 : Genetic Counselling The couple is offered detailed Genetic Counselling by LifeCell's board-certified Genetic Counsellors.

Step 3 : Pre-PGT Workup Each PGT-M test design is unique and specific to the family, so DNA samples from both partners, and often additional family members, will be requested in order to design a test. The TRF and informed consent is submitted to the Lab. Genetic markers that are informative, flank the locus of interest and allow discrimination of the parental haplotypes are selected for use in the clinical test. The test is run on both blood samples and WGA products for high-confidence validation. Once a reliable test is successfully developed, the lab sends a confirmation to the Clinician.

Step 4 : IVF For fertilisation, ICSI must be used to avoid contamination by the sperm. IVF is performed and the resulting embryos are biopsied and vitrified. Pre-ordered collection kits are used for transportation.

Step 5 : PGT-M The Embryo biopsy samples received at the lab are analysed for the presence of mutations and results are released to the IVF centre.

Step 6 : Embryo Transfer Based on the results, the transfer of unaffected embryos is performed.



Possible PGT-M Results

UNAFFECTED

An embryo with normal PGT-M results is predicted to be free of the genetic condition for which it was tested. Therefore, it is recommended for transfer.

CARRIER

For autosomal recessive conditions, PGT-M will also identify a carrier embryo. Since carriers are not expected to have symptoms, those embryos may be transferred if the couple wishes.

AFFECTED

The embryo is expected to be affected with the condition for which it was tested. Therefore, these embryos are typically not recommended for transfer.

PGT-M Coupled with PGT-A

Due to the high rate of sporadic chromosome abnormalities in embryos (30-80%, depending on maternal age), even from healthy, young, or fertile individuals, PGT-A can provide valuable information and help us find the embryos that are most likely to result in a successful pregnancy. These tests can be done simultaneously on the same biopsy, and adding PGT-A to a PGT-M IVF cycle does not change the overall process or the timeline for results.

Choose the assurance of PGT-M and confidence of PGT-A together to maximize the chance of implantation followed by a healthy live birth.

Entire Range of Genetic Testing Options to complement the IVF journeys

- Male and Female Infertility Carrier Screening, Donor Screening
- Biopsy Training Support
- Prenatal Screening and Diagnostics Testing Solutions
- Dedicated and Prioritized Logistics Support
- Laser Machine and Technician Support
- Complimentary Genetic Counseling with Clinical Geneticists and Board Certified Genetic Counsellors

As per ACOG Committee Opinion Number 799 "Preimplantation genetic testing-monogenic uses only a few cells from the early embryo, usually at the blastocyst stage, and misdiagnosis is possible but rare with modern techniques. Confirmation of preimplantation genetic testing results with traditional screening for aneuploidy or diagnostic testing for PGT-A is recommended for all patients. For PGT-SR and PGT-M diagnostic testing by chorionic villus sampling (CVS) or amniocentesis should be offered to all patients.

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