merrion
FERTILITY CLINIC

PGT-M

Preimplantation Genetic Testing for Monogenic or Single Gene Disorders

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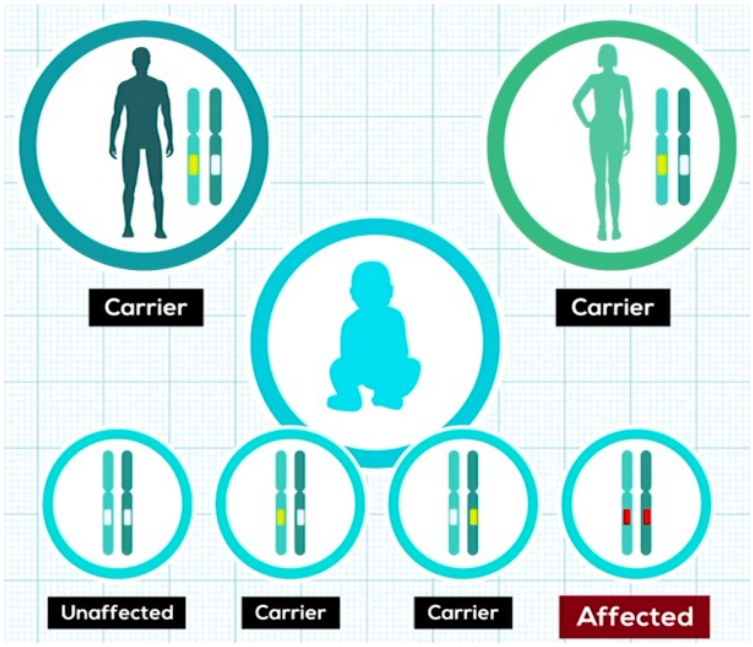
Introduction

PGT-M, also known as Preimplantation Genetic Testing for Monogenic or Single Gene Disorders, is a genetic test performed on embryos produced through IVF, or in vitro fertilisation. PGT-M provides information about embryo genetic health for those who are at a known increased risk of having a child with a specific genetic disorder. This information helps you and your clinical team identify an embryo to transfer that is free of the genetic disorder in question. PGT-M may be referred to as PGD or Preimplantation Genetic Diagnosis. While you may hear and see these different names, these are all the same test.

You may consider PGT-M if,

- **You have a genetic disorder yourself.**
- **You have a family member with a genetic disorder.**
- **You have had a previous pregnancy or child with a genetic disorder.**
- **You and/or your partner are known carriers of a genetic disorder.**

Being a carrier means that you are not typically affected by the genetic condition itself but depending on the specific disorder, you may have an increased risk of having a child with that condition.



(Figure 1. Graphic detailing how genetic disorders can be inherited)

Common conditions that PGT-M is performed for include,

- Cystic fibrosis
- Fragile X syndrome
- BRCA-1 and BRCA-2 related cancer syndrome.
- Thalassemia
- Huntington's disease

The test may not be able to identify all potential mutations associated with a given condition and/ or those that may lead to unsuccessful outcomes.

Getting Started

The PGT-M process begins with a referral from your doctor. The PGT laboratory will evaluate any provided genetic reports to determine if PGT-M may be appropriate for you. You may be scheduled to speak with a genetic counsellor at the lab to discuss your case in more detail. The genetic counsellor will discuss the testing process with you, assess your personal and family medical history and review the condition that you are pursuing PGT-M for.

Every PGT-M test is custom created uniquely for each family. Often you, your partner, and additional family members will need to provide genetic testing results and DNA samples in order to develop and validate your custom test.

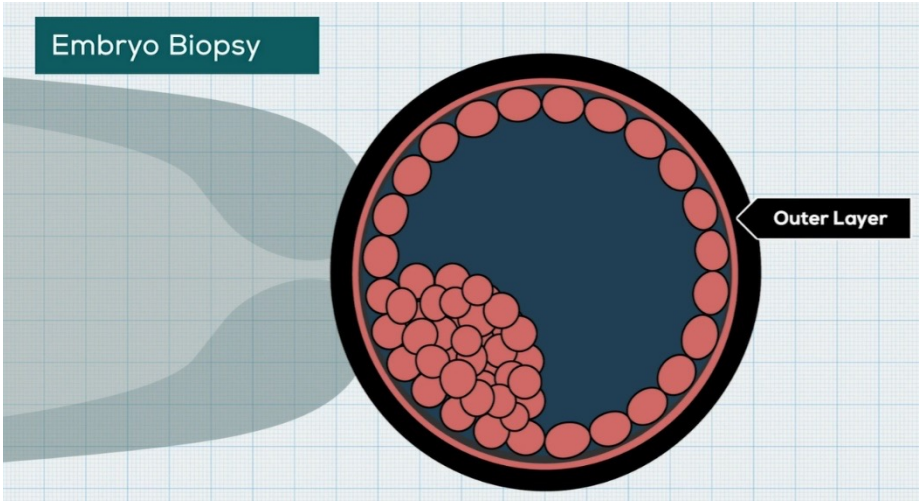
One benefit of this customised test is that PGT-M can be performed for most single gene disorders, when the genetic condition is harmful, the specific familial mutation has been identified and appropriate family members are available to participate in the PGT process.

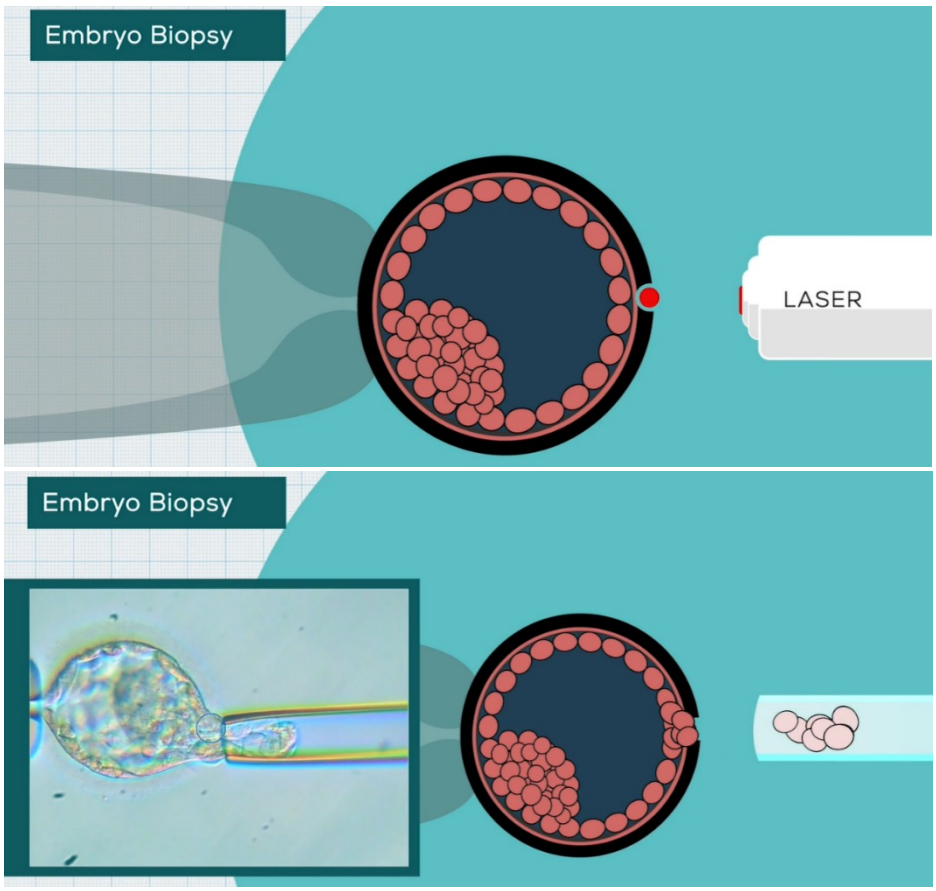
Embryo Biopsy

After the genetic testing laboratory reviews and accepts your case, they will work with you to develop your custom PGT-M test. Once development is complete you may begin your IVF cycle.

To perform PGT-M, a small number of cells are removed from the embryo via a biopsy. This sample is sent to a specialised genetics laboratory for analysis. The lab Merrion Fertility Clinic use is Cooper Genomics, which is based in the UK. Embryos are typically biopsied on day 5, day 6 or day 7 after egg retrieval. Only embryos with satisfactory quality that continue developing to this stage are tested. By this time the embryo contains over 100 cells, and several cells can be removed from the outer layer of the embryo (trophectoderm), which is the part of the embryo that will eventually become the placenta. No cells are taken from the inner cell mass, the part of the embryo that will develop to become the foetus.

In order to most effectively remove these cells without damaging the embryo, a highly skilled embryologist will make a small hole in the shell of the embryo and use an instrument that is less than 1/10th the diameter of a human hair to carefully perform the biopsy.





(Figure 2. Steps involved in an embryo biopsy for PGT)

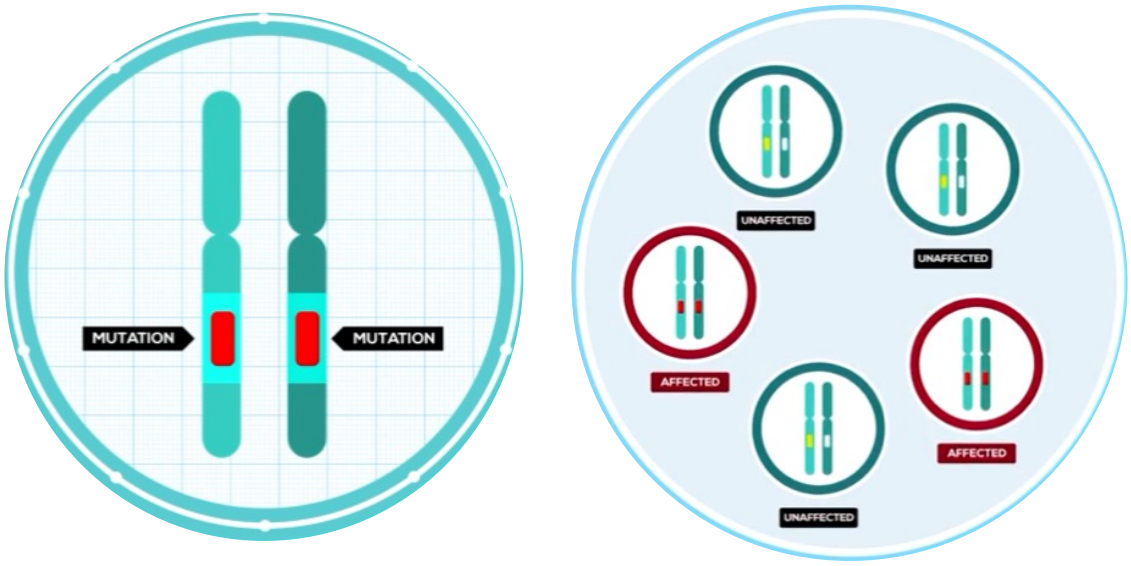
The cells obtained from the biopsy are then washed to remove any potential sources of contamination and transferred into small tubes and sent to the CooperGenomics laboratory for analysis. Only the biopsy sample is sent off site. The embryos remain at Merrion Fertility Clinic and are cryopreserved until the PGT-M results are returned.

Thus far, babies born after procedures that include embryo biopsy have not had an increased rate of birth defects. Although data has shown that embryo biopsy has no adverse impact on growth or medical outcomes, there is potential for unknown consequences to live born babies.

An embryo may be damaged during biopsy, which will cause it to not be suitable for transfer. With a skilled embryologist, the risk of damaging an embryo is very low. While it is important to understand the risks involved in the process, embryos have been biopsied for over 25 years and have resulted in tens of thousands of healthy pregnancies.

PGT-M Analysis

Once the biopsied cells arrive at the genetic testing laboratory, PGT-M is performed using a technique called karyomapping. Karyomapping allows the scientists to look at the region of the genes surrounding the specific mutation to determine whether each embryo is affected with the condition or not.
The results from this test will help the clinical team at Merrion Fertility Clinic determine which embryo to transfer.



(Fig 3. Karyomapping analysis)

Depending on the specific condition you are performing PGT-M for, the possible results can vary. A genetic counsellor can help you understand your results, helping you and your doctor make informed transfer decisions. If unaffected embryos are available, a frozen embryo transfer cycle can then be performed.

Embryo Transfer

The benefit of PGT-M is that by knowing whether an embryo has a genetic disorder or not, you can avoid transferring an abnormal embryo. With the information provided by PGT-M, it is recommended that a single embryo is

transferred as the pregnancy rate per transfer is increased and the miscarriage rate is decreased. With PGT-M, the risk of an ongoing pregnancy having a genetic problem is significantly reduced.

PGT-M Limitations

PGT-M cannot guarantee the birth of a chromosomally or genetically normal child and is not a replacement for prenatal testing. In fact, prenatal testing should be considered for all pregnancies resulting from PGT-M. PGT involves biopsying and testing cells taken from the trophectoderm (the cells that will become the placenta) and not the inner cell mass (the cluster of cells that will become the fetus). Therefore, it is possible that the genetic profile of the cells tested may vary from the cells that will form the fetus.

It's important to understand the benefits, risks, and alternative options, in order to make an informed decision about pursuing PGT-M. While there is some risk involved, technological advances have made PGT-M an effective tool for improving IVF success rates.

In extremely rare cases, human error, or natural forces beyond the control of Merrion Fertility Clinic or Cooper Genomics, such as weather and air travel issues, can result in an inability to perform testing and receive results. Remember, even in this rare scenario, only the sample that was biopsied is impacted. Your embryos will still be safe at Merrion Fertility Clinic.

Lastly, sexual intercourse during treatment may result in a spontaneous pregnancy. Sperm from intercourse may result in fertilisation and implantation in addition to, or instead of, fertilisation and implantation from treatment. This would invalidate the results from PGT. Please consult with the Merrion Fertility Clinic team about timing of sexual intercourse during your treatment.

For more information about PGT-M, please contact Merrion Fertility Clinic.