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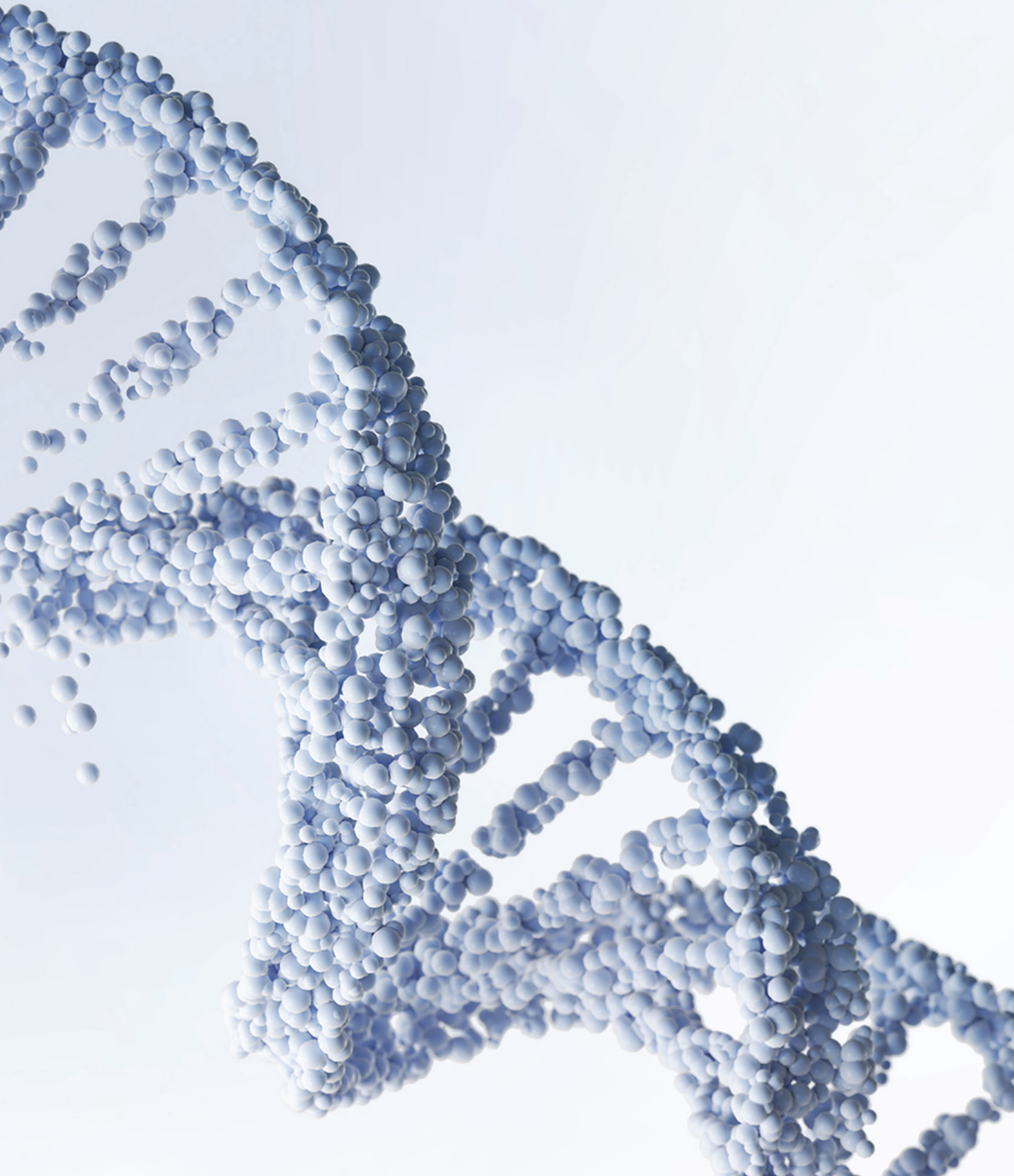
WORLD LEADING FERTILITY

# PGT-M

## Pre-implantation Genetic Testing for Monogenic Conditions



# What is Pre-implantation Genetic Testing (PGT)?

Genea's PGT scientists have helped hundreds of families maximise the potential of having a healthy baby. Chromosome screening of embryos was launched in 1996, with testing for inherited single gene disorders introduced in 1998. Since then, our PGT techniques have continued to be world leading. Genea is one of the very few centres in Australia that has both IVF and genetics facilities onsite to perform these sophisticated tests successfully.

Embryos are first created via IVF and then Genea's PGT assays are used to select those free from chromosomal issues (such as unbalanced translocations) or familial single gene disorders (eg. cystic fibrosis, spinal muscular atrophy). By choosing embryos which have had genetic screening, you will increase the chances of a healthy ongoing pregnancy and birth of an unaffected child.

# Single Gene Disorders (also known as Monogenic Conditions)

Our chromosomes contain around 20,000 pairs of genes in total. Genes are the instructions for how our bodies grow and function. Sometimes there can be variations in a gene which cause the gene to not function properly, leading to health issues. This is known as a single gene disorder. Examples of genetic conditions which are single gene disorders include cystic fibrosis, neurofibromatosis and Duchenne muscular dystrophy.

Individuals with a personal or family history of a single gene disorder may have an increased chance of having a child affected with the condition. However, even people with no history can still be at risk. For this reason, prior to starting a family, many reproductive couples are now choosing to have preconception or reproductive carrier screening to see if they carry genetic variants that put them at risk of having a child with health issues.

# Preimplantation Genetic Testing for Monogenic Conditions (PGT-M)

PGT-M is a genetic test that can be performed in embryos created via IVF when an individual or couple are known to have an increased risk of a specific single gene disorder. Once the embryos are at a suitable stage of development, a small number of cells are carefully extracted for analysis.

PGT-M allows you to reduce the risk of having a child affected with the single gene disorder in your family. Genea PGT Scientists have experience in testing embryos for over 350 common and rare genetic conditions such as inherited breast cancers, thalassemia or Huntington disease.

For PGT-M to be an option, the specific genetic cause needs to have already been identified in your family through molecular genetic testing. If there is no genetic variant identified in you or your affected family member, testing of embryos may not be possible.

The Genea Genetics team can provide advice based on your individual circumstances. We have techniques which allow PGT to be an accurate testing option for most couples.

**PGT-M may be appropriate in the following circumstances:**

- An individual has a personal or family history of a confirmed genetic diagnosis where there is a risk of passing on a serious health issue to their children, such as neurofibromatosis.
- One or both reproductive partners are carriers of single gene conditions that may affect health of a future child, such as conditions picked up on reproductive carrier screening like spinal muscular atrophy and fragile X syndrome.

Genea's PGT-M techniques also include a chromosomal screen for aneuploidy. Many embryos are aneuploid and this is not related to family history. Please refer to Genea's Preimplantation Genetic Testing for Aneuploidy booklet for more details about chromosome screening of your embryo.

PGT-M is not a screen of an embryo for all known genetic conditions, only for the condition that is confirmed via a diagnostic genetic test in your family.

# Leading technology to select the best embryo

Every time an IVF cycle produces more than one embryo, embryologists must make a choice about which embryo will be transferred.

**Standard IVF**
Selection based on appearance of the embryo.

**Genea PGT-M**
Selection based on genetic make-up with the appearance of the embryo used as a secondary criteria.

# Your Genea Pre-implantation Genetic Testing (PGT) Treatment Timeline

**What are the steps involved to do PGT-M?**

Genetic screening and your individual circumstances should be discussed with your Fertility Specialist before commencing treatment, but as a general guide:

1. **Fertility Specialist** - After a discussion with a Genea Fertility Specialist, a referral will be sent to the Genea Geneticist and PGT Scientists.

2. **Genetics team** – An appointment will be booked with a Genea Geneticist after relevant genetic test reports are obtained. The PGT Scientists will contact you regarding the PGT test design work up and sample requirements. They will send a DNA collection kit to collect samples from you and possibly other family members.

3. **Geneticists** – The Geneticist will meet with you (via zoom or face to face) to discuss the PGT-M method and process specifically related to the condition being tested and Genea's testing techniques.

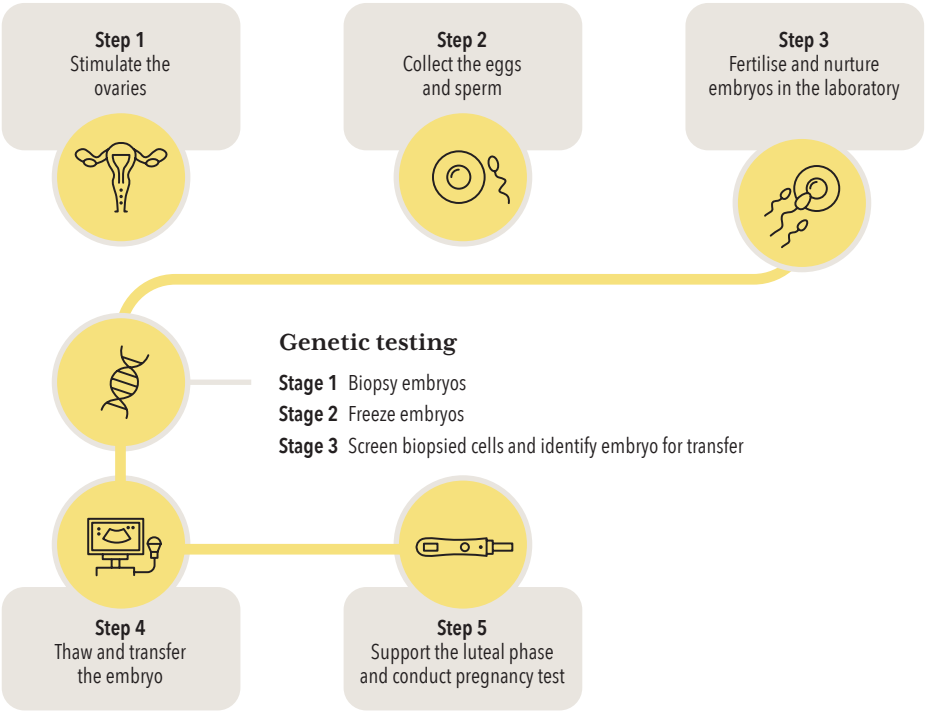
4. **Patient Relationship Coordinators** – If you wish to proceed, you will be connected to a Genea Patient Relationship Coordinator (PRC) who will take the work-up payment and notify the scientists to initiate the test work-up.

5. **PGT-M work-up** – During this time, scientists will design and validate a PGT test for your embryos specific to the condition in you/your family. The test work up can take 6-12 weeks depending on your circumstances and should be finished before you start an IVF cycle.

6. **Nursing Consult** – Your treating Genea clinic will book your nursing consult when your work up is near completion. Nurses discuss the timeline of your cycle, medications, blood tests and ultrasounds required and what is expected during an egg collection.

7. **Start IVF** – The PGT scientists will inform you when the work up is complete and the PRCs will contact you to provide a fee estimate for your IVF cycle.

# What is involved in testing of embryos?




Embryos will be grown in the laboratory for 5-6 days until they reach the blastocyst stage. Embryos either start hatching on their own, or require assisted hatching. Assisted hatching is performed either on day 4 or at the time of the biopsy.

The embryology team will assess whether your embryos are suitable for an embryo biopsy and PGT-M testing and provide you with an update.

An embryo biopsy is performed by removing a small sample of hatching cells (less than 5 per cent) from the trophectoderm (the outside structure of the embryo that becomes the placenta in an ongoing pregnancy). It is normal for some of your embryos to not develop sufficiently and therefore be unsuitable for testing or freezing.

All biopsied embryos will be frozen to allow sufficient time to perform the PGT tests. Please note, a fresh embryo transfer will not be possible if you want all your embryos to undergo PGT-M testing.

# PGT Results

Results will be available approximately three weeks after your embryo is biopsied, at which time a PGT scientist, genetic counsellor, your Fertility Specialist, or an embryologist will call you to discuss the results.

A copy of these results will also be sent to your Fertility Specialist who will discuss your treatment options and next steps.

## Results explained

**No Abnormality Detected (NAD)**
The embryo is not affected with the condition tested, has a balanced number of chromosomes, and is available for transfer.

**Abnormal (ABN) / Affected (AFF)**
The embryo is affected with the condition tested and/or has an unbalanced number of chromosomes. It will not be available for transfer.

**Mosaic Embryo**
This means that some cells in the embryo have the wrong number of chromosomes and some cells have the standard number of chromosomes. Mosaic embryos have a reduced chance of implantation and live birth and higher chance of miscarriage. Outcome data shows that mosaic embryos have the potential to lead to a healthy ongoing pregnancy and Genea allows transfer of mosaic embryos after a detailed discussion with one of our Genetic Counsellors. The vast majority of mosaic embryos are due to random errors, they are not caused by chromosomal rearrangements.

**Unknown (UNK)**
No result was obtained due to sample or testing issues. You may be asked if you would like to re-biopsy the embryo and try to test again. This will reduce the quality and success rates of transferring this embryo.

Rarely, there may be results where there is uncertainty and further testing or interpretation may be required, which will be discussed with you.

### Can I transfer an abnormal of affected embryo if I have no other embryos to transfer?

It is a Genea policy that for an embryo that has been tested and reported as abnormal or affected, this embryo is not available for transfer. Affected embryos will be discarded as per current local recommendations.

### Prenatal screening - Should you have prenatal diagnostic tests done?

Whilst PGT-M does have a high degree of accuracy, it will never be 100 percent due to various biological factors and technical difficulties that can be experienced. Our geneticist or genetic counsellor can provide more detail on the accuracy based on your individual circumstances. We recommend that prenatal screening and diagnostic tests are discussed with your referring fertility doctor.

Clinical interpretation provided in the results will be current as of the date the test is performed and reported. Clinical interpretation of test results can change over time with emerging data and/or changes in professional organization guidelines. Genea is under no obligation to review and update results in response to these changes.

# What you need to know

- Testing will reduce the number of embryos available for transfer, but will ensure those that are transferred have the best chance of survival and a healthy pregnancy.
- You may have an embryo that is not suitable for testing.
- Embryos must be frozen pending test results, which are usually available in 3 weeks.
- It is possible that all of your embryos have an abnormality and/or be affected for the condition for which we are testing, resulting in no embryos being suitable for transfer from your IVF cycle. Embryos reported as affected will not be available for transfer at a Genea clinic.
- Due to technical limitations of the testing process, it is possible that some embryos do not achieve a result.
- An embryo may return a result indicating a mixture of abnormal and normal cells (referred to as mosaicism) and may be able to be transferred after a discussion with a genetic counsellor.
- The test does not detect all types of genetic abnormalities and standard prenatal screening is recommended in an ongoing pregnancy.
- There is no guarantee a tested embryo will result in a pregnancy.
- PGT-M embryos are reported as affected based on the current understanding of how the gene variants tested are associated with the condition and it's severity.
- Unless specifically requested otherwise, affected embryos will be discarded as per current local regulations regarding the transfer and discarding of affected embryos.

If you have any questions, please do not hesitate to contact a Genea Genetic Counsellor on **(02) 8484 6548**.

For more detailed information about costs, suitable Genea Fertility Specialists, and next steps please contact the Fertility Concierge on **(02) 8484 7666**.

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