

Monash IVF

Fact Sheet

Preimplantation Genetic Diagnosis (PGD) for Single Gene Disorders



Key points:

- Individuals with a family history of a single gene disorder may be at risk for passing this disorder on to their children.
- Preimplantation Genetic Diagnosis (PGD) is a reproductive option for couples at risk of passing on a specific single gene disorder to their child, and significantly increases the chance of having a healthy baby.
- One or both partners must have had previous genetic testing to determine the gene change/s causing the genetic disorder in their family.
- PGD is NOT 100% accurate. Confirmatory prenatal diagnosis is highly recommended if a pregnancy is achieved following PGD.

What is a single gene disorder?

Single gene disorders are genetic conditions which are caused by specific gene change/s in a person's DNA. Single gene disorders are heritable and often run in families. Individuals with a family history of a single gene disorder may be at risk for passing the condition onto their children. Examples of single gene disorders include Cystic Fibrosis, Huntington Disease, Fragile X and Myotonic Dystrophy.

How is this test done?

Step 1: Genetic testing

One or both partners must have had previous genetic testing to determine the exact gene change/s causing the genetic condition in their family. If the causative gene change/s has not yet been identified, the couple should be referred to Genetic Health Services Victoria (phone +61 03 9594 2026), where genetic specialists will be able to organise this genetic testing. The PGD team need to know the causative gene change/s in order to proceed with developing a PGD test.

Step 2: Genetic counselling in PGD clinic

Once the specific gene change has been identified, the couple should make an appointment to attend the Monash IVF PGD clinic. During this appointment the couple will be provided with information on the PGD program at Monash IVF and will have an opportunity to have any questions answered.

Step 3: Feasibility testing

Prior to commencement of an IVF/PGD cycle, it is necessary for the couple to undergo feasibility testing in order to determine if PGD will be possible for their particular genetic condition. Feasibility testing will require a blood sample from both partners. The genetic counsellor will organise for the collection of these samples following the PGD clinic appointment. In most cases, a blood or DNA sample will also be required from one of the following:

- Both partner's parents
- The couple's child
- A DNA sample from prenatal testing in a previous pregnancy

These additional samples are used to track the inheritance of the particular gene change/s within the family.

Feasibility testing is required to ensure that the Monash IVF PGD laboratory is able to develop a test that can detect the specific gene change/s. The feasibility process also ensures that this test is sensitive enough to provide a result from a single cell.

In most cases, specific "linked markers" are included in the final test in order to increase the accuracy of the results. Linked markers are segments of DNA that are located close to the specific gene of interest and are

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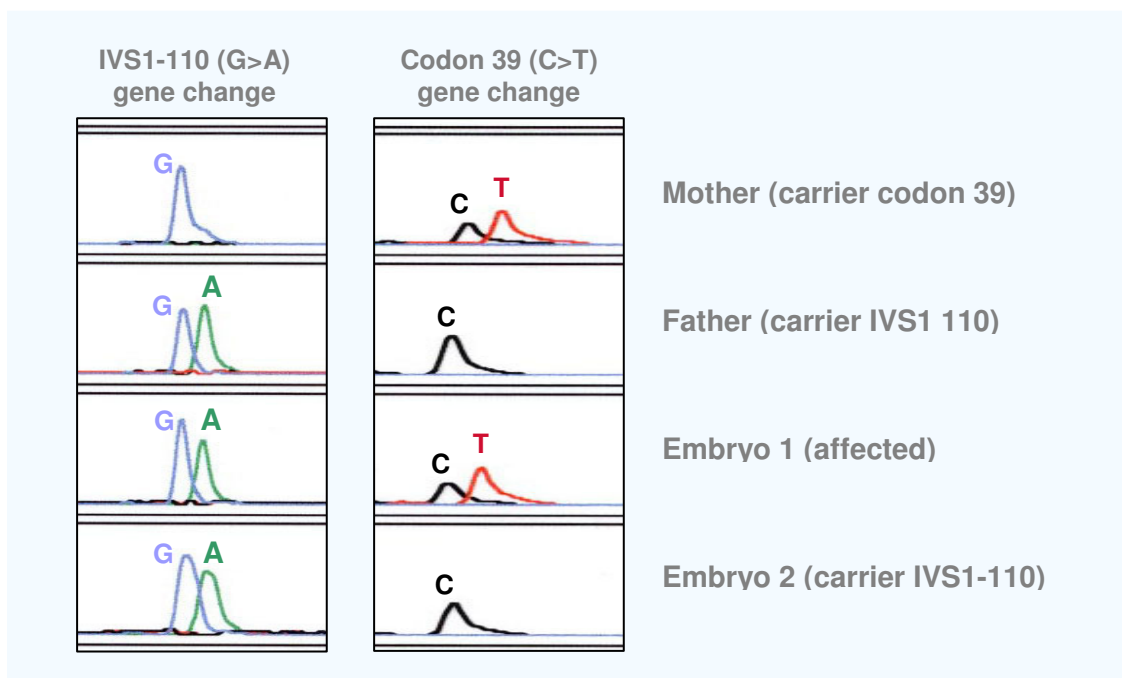
usually inherited together with the gene. Ideally, each partner will have different marker sizes which will enable the PGD laboratory to distinguish between each gene copy. These markers are used to confirm the result of the direct gene testing.

A feasibility report outlining the results of the feasibility testing is sent to the IVF doctor and genetic counsellor. The genetic counsellor will contact the couple to go through the results of the feasibility testing process. In some instances an accurate test may not be possible to develop and PGD may not be available. There is a non-refundable fee for the feasibility test. If feasibility has been confirmed, IVF/PGD may proceed.

Step 4: IVF/PGD Cycle

Once feasibility testing has been completed and PGD is feasible, the couple are able to undertake an IVF/PGD cycle. Embryo biopsy is performed on Day 3 after egg collection (please refer to the "Preimplantation Genetic Diagnosis" fact sheet for further information relating to the embryo biopsy and PGD procedure). The biopsied cells are tested using a technique called fluorescent polymerase chain reaction (F-PCR). F-PCR makes millions of copies of the relevant region of DNA so that a reliable diagnosis can be made on each embryo. The product from the F-PCR reaction is tested for the presence or absence of the known parental gene change/s using a range of genetic techniques and a genetic analyser (Figure 1). Final results are usually obtained 12 to 24 hours after biopsy. The embryo is kept in culture while the testing of the biopsied cells proceeds. Embryos identified as being unaffected by the disorder are transferred to the uterus on Day 5. A qualified PGD scientist will discuss the PGD results with the couple prior to transfer.

Figure 1: Example of single gene PGD results



When a number of unaffected embryos are identified, morphological criteria are also used to determine those best for transfer. Surplus unaffected embryos will be grown in culture to Day 5 or Day 6. If they reach an appropriate stage of development (ie: form a blastocyst), they will be frozen. These embryos may be used in a subsequent IVF cycle if a pregnancy is not achieved with the fresh embryos. Affected embryos are discarded or donated to research/training with the couple's consent.

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Other important information

- Due to the complexity of the genetic tests, it may not be possible to obtain a conclusive result for some or all embryos. In this case, the embryos can either be transferred without a genetic result or frozen if they reach an appropriate stage of development (ie: form a blastocyst). It is possible that a second biopsy procedure (called blastocyst biopsy) can be performed on these embryos to try and obtain a conclusive genetic result. This may require an additional PGD fee. If blastocyst biopsy is possible and unaffected embryos are identified, these can be transferred in a frozen embryo transfer cycle.
- The PGD test is specifically designed to test for the gene change/s that have previously been identified in one or both partners. The test does not give any information relating to other gene changes within the same gene, other single gene disorders, or chromosomal abnormalities.
- The accuracy of the test is detailed in the feasibility report that is sent to the couple's IVF doctor. Many factors influence the accuracy of the test, including the nature of the gene change/s, the number of cells biopsied from the embryo and the clarity of the results obtained. While every effort is made to ensure that the PGD test offered has the highest possible accuracy using the currently available technology, an error rate of 2-10% is associated with this testing. **Prenatal diagnosis is highly recommended in an ensuing pregnancy.**

What are the costs?

Information relating to the cost of PGD is available from Monash IVF. Please note that additional costs will be incurred for IVF.

Quality systems

Monash IVF employs a very high standard of quality assurance. Through the application of quality systems the laboratory provides standards of excellence in quality service, care and advice.