Monash IVF
Fact Sheet

Preimplantation Genetic Diagnosis (PGD) for Translocations

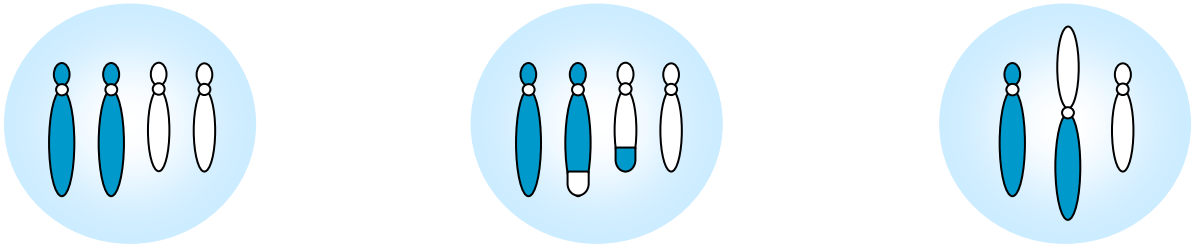
Key points:

- Translocation carriers are at risk of producing embryos which are unbalanced for the translocation chromosomes.
- Chromosomally unbalanced embryos will fail to implant, miscarry, or result in the birth of a child with a chromosome abnormality.
- Preimplantation Genetic Diagnosis (PGD) with translocation testing can be used to distinguish between "normal/balanced" embryos and "unbalanced" embryos. Only embryos which are "normal/balanced" for the translocation chromosomes are considered suitable for transfer to the uterus.
- PGD is NOT 100% accurate. Confirmatory prenatal diagnosis is highly recommended if a pregnancy is achieved following PGD.

What is a translocation?

An individuals genetic information is packaged into strings of DNA called chromosomes. Normal human cells contain 46 chromosomes, or 23 chromosome pairs. These chromosome pairs are labelled 1 to 22 (the autosomes) and X and Y (the sex chromosomes). A translocation is a rearrangement of chromosome segments between two different chromosomes. These translocations may be either reciprocal translocations, involving reciprocal exchange of segments between chromosomes, or Robertsonian translocations, involving a whole arm exchange between chromosomes (Figure 1).

Figure 1: Different types of translocations.



Normal Chromosomes | Reciprocal Translocation | Robertsonian Translocation

Carriers of these translocations are considered "balanced" because all their genetic information is present. However, they are at risk of producing sperm or eggs with an "unbalanced" form of their translocation. This may result in difficulty to conceive, recurrent miscarriages or the birth of a child with a chromosome abnormality. PGD testing can be used to distinguish between "normal/balanced" embryos (which have the potential to result in a successful pregnancy) and "unbalanced" embryos (which would fail to implant, miscarry, or result in the birth of a child with a chromosomal abnormality).

How is this test done?

Step 1: Chromosome testing

One or both partners must have been found to carry a translocation. The PGD team need to know the precise translocation in order to try to develop a PGD test.

Step 2: Genetic counselling in PGD clinic

Once the specific translocation 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.

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Step 3: Feasibility testing

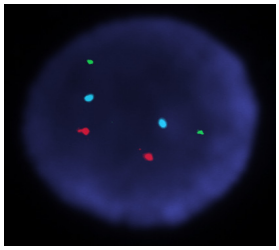
Prior to commencement of an IVF/PGD cycle, it is necessary for the couple to undergo a feasibility test in order to determine if PGD will be possible for their particular translocation. Most carriers of a reciprocal translocation have a unique chromosome rearrangement and therefore a new FISH test must be developed for every couple. Feasibility testing will require a blood sample from both partners. The genetic counsellor can organise for the collection of these samples following the PGD clinic appointment. Cells will be extracted from this blood sample and will be used in the feasibility testing process. During the feasibility testing process, the PGD scientists identify a set of DNA probes which are capable of distinguishing between embryos which are "normal/balanced" for the translocation chromosomes and embryos which are "unbalanced" for the translocation chromosomes. Once an accurate test has been developed using this set of probes, it will be validated on cells from embryos which have been donated for succumbed research and training. This will help the Monash IVF PGD laboratory to ensure that the final test is sensitive enough to provide a result from a single cell from an IVF embryo.

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.

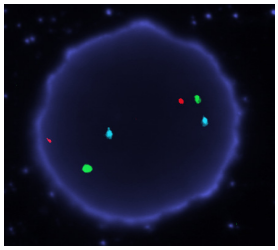
Step 4: IVF/PGD cycle

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 Fluorescence In Situ Hybridisation (FISH). Fluorescent dyes are used to tag the specific chromosomes involved in the translocation. These tags show as coloured dots which can be used to indicate whether the embryo is "normal/balanced" for the translocation chromosomes or carries an "unbalanced" form of the translocation (Figure 2). Final results are usually obtained 24 hours after biopsy. The embryo is kept in culture while testing of the biopsied cell/s proceeds. Embryos identified as being "normal/balanced" for the translocation chromosomes can be transferred on Day 5. A qualified PGD scientist will discuss the PGD results with the couple prior to transfer. This process should increase the chance of a successful pregnancy and significantly reduce the risk of miscarriage.

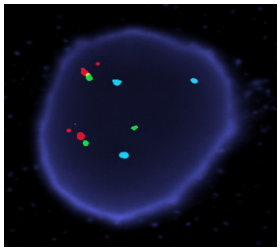
Figure 2: Examples of FISH analysis for a reciprocal translocation. "Normal/balanced" cells should have two red signals, two green signals and two aqua signals.



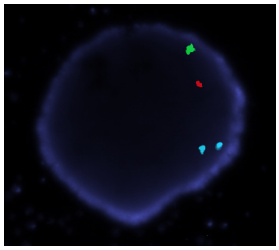
Parental Profile (Carrier)



Embryo One (Normal/Balanced)



Embryo Two (Unbalanced)



Embryo Three (Unbalanced)

When a number of "normal/balanced" embryos are identified, morphological criteria are also used to determine those best for transfer. Surplus "normal/balanced" embryos which are not transferred but which continue to develop satisfactorily to the blastocyst stage may be frozen. These embryos may be used in a subsequent IVF cycle if a pregnancy is not achieved with the fresh embryos. Chromosomally abnormal embryos are discarded or donated to research/training with the couple's consent.

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Other important information

- PGD cannot distinguish between “normal” and “balanced” embryos.
- Due to the complexity of FISH testing 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).
- PGD with translocation testing involves analysis of the translocation chromosomes. The test does not give any information relating to other chromosomes, other genetic conditions or other abnormalities. However, in some cases it may also be possible to perform aneuploidy screening for a limited number of chromosomes (ie: 13, 18, 21, X and Y; refer to the PGD with Aneuploidy Screening fact sheet for further information). This additional testing will only be performed upon request and will incur an additional fee.
- This test is only a screening test and therefore cannot provide an absolute guarantee of the chromosome status of the embryo. Given the complexity of the testing, an error rate of approximately 10% is associated with this test. Therefore, **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.