Preimplantation Genetic Diagnosis

What is preimplantation genetic diagnosis (PGD)?

In a normal IVF cycle, your embryologist chooses which embryo (or embryos) will be transferred to the uterus based on visual observation of the embryos as they develop. Preimplantation genetic diagnosis (PGD) allows the scientist to base their choice on the results of detailed genetic tests on the embryos, excluding those embryos that contain an obvious genetic abnormality.

For example, when two cystic fibrosis carriers conceive a child, there is a 25% chance that the baby will have cystic fibrosis, a 50% chance that the baby will be a carrier and a 25% chance that the baby will be unaffected. IVF with PGD allows the couple to produce a number of embryos, but to transfer only those that are either unaffected or carriers.

Genea is one of the very few centres in Australia that successfully has the combination of IVF and genetics facilities to perform these sophisticated tests.

Types of genetic disease

There are four kinds of genetic diseases.

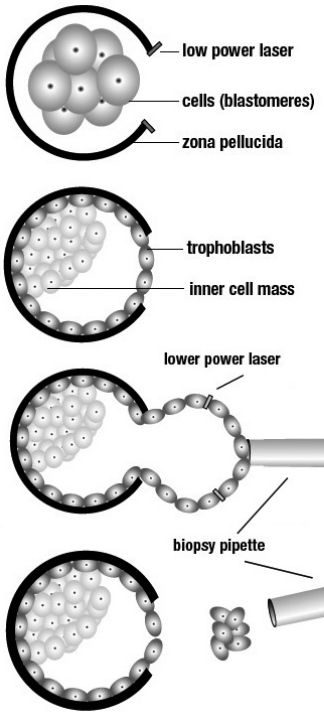
1. Chromosome errors e.g. Down syndrome, translocations
2. Errors within a gene
   e.g. cystic fibrosis, myotonic dystrophy
3. Errors within the mitochondria
4. Errors in more than one gene

How is PGD done?

The biopsy

You will need to have an IVF cycle to create embryos, just like couples with infertility undergoing an IVF cycle.

PGD requires the biopsy (or removal) of cells from each embryo for analysis. At Genea, our advanced embryo culture techniques allow us to wait until the embryos have reached their fifth day of development (known as 'blastocyst' stage) when they can have a hundred or more cells, and remove three to four.



At Day 3 of the embryo's development, a small hole is made in the outer layer of the embryo (the 'zona pellucida') using a delicate laser beam.

The embryo continues development until Day 5 or 6 when it becomes a blastocyst, characterised by the separation of cells into trophoblasts (which go on to become the placenta) and the inner cell mass (which go on to become the fetus).

Trophoblasts are drawn out through the hole using a hollow suction tube called a biopsy pipette.

The required cells are separated from the others using the laser and collected separately.

The remaining cells quickly realign and the embryo goes on developing.

The analysis

The removed cells have not yet differentiated into the specific tissues of the body. Every one of an embryo's cells has a full complement of the embryos genetic information, this is important for two reasons:

1. Cells can be removed from an embryo and the embryo can still continue to develop normally. (A small proportion do not survive the biopsy.)
2. Cells removed for analysis are usually representative of all the cells in the embryo. i.e. if the cell's genetic material is abnormal, the embryo is abnormal. (There is a condition called 'mosaicism' where this is not the case.)

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Genea scientists use a number of different methods to analyse the biopsied cells. The most common are Comparative Genome Hybridisation (CGH) and polymerase chain reaction (PCR).

CGH

CGH is a process that allows us to look at all 24 chromosome types in an embryo. Female = 46, XX.
Male = 46, XY. The process takes several days to achieve results therefore all embryos need to be vitrified.
Cryo embryo transfer in subsequent cycle.

PCR

If the problem is at a gene level, rather than chromosome, it is more common to use PCR. PCR makes millions of copies of a part of the DNA code, enabling us to see whether this part of the DNA in the sample is normal.

For example, if cystic fibrosis (which is caused by a mutation of a particular gene) were suspected, PCR would show us whether that gene was normal or mutated.

Who can benefit from PGD?

If you have or carry a diagnosed genetic problem, you can discuss whether PGD is applicable with your geneticist or physician, or by calling Genea.

Risks of embryo biopsy

The removal of a cell (sometimes two cells) from a Day 3 (usually 8-cell) embryo can possibly stop the development of the embryo, before or after it is transferred. This seems to be less likely with Day 5 or Day 6 (blastocyst-stage) biopsies. So far, there is no evidence to suggest that embryo biopsies cause birth defects.

Is the result always correct?

For most scientific and medical tests there is a small risk of an abnormal result when there is no abnormality (false positive) or a normal result when there is really an abnormality (false negative). From published studies and our own research, we know that the chance of a false result for CGH is 5%. A chance of a false result for a PCR test is usually less than 1%, but varies for each family.

As well, your fetus or baby might be at risk for other conditions that have not been looked for. You should therefore still discuss prenatal testing with your obstetrician.

Will we always get a result?

Genea is able to determine the genetic status in more than 95% of embryos tested.

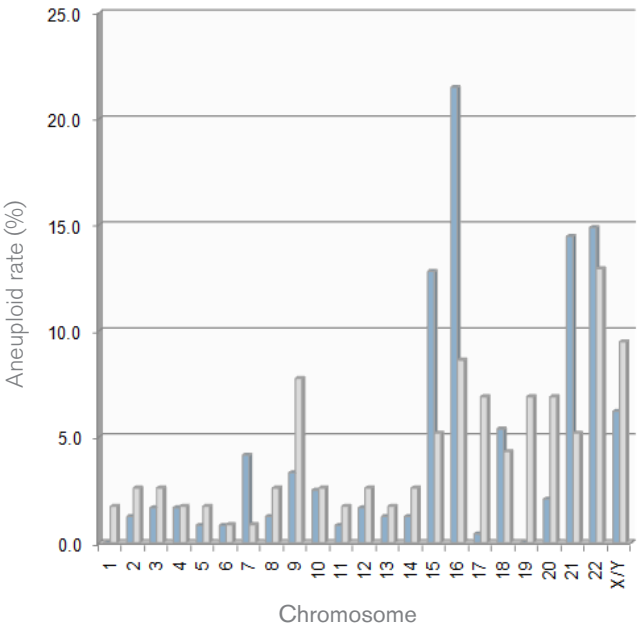
PGD in regional NSW and ACT

PGD is offered at our clinics in Wollongong, Newcastle, Liverpool and Canberra.

Getting started on an IVF cycle for PGD

1. Obtain a referral to a Genea specialist who will be responsible for your care. A list of accredited doctors is available on our website www.genea.com.au
2. Ring the nurse coordinator who will arrange:
   - appointment with Genea specialist
   - appointment with clinical geneticist
   - interview with nurse coordinator and scientist
   - appointment with counsellor

Aneuploid chromosomes



A comparison of chromosome aneuploidies in IVF miscarriage samples and PGD embryos.

- IVF miscarriage samples
- PGD Embryos

Pregnancy* rates following the transfer of PGD tested embryos

Year	Fetal heart pregnancy outcomes per transfer cycle (%)	
	Fresh transfer	Frozen transfer**
2010	39.3%	36.3%
2011	42.1%	37.1%
2012 (Jan to Nov)	49.2%	48.4%

*Pregnancy defined as a positive fetal heart at 7 week ultrasound.
**All CGH tested embryos are captured in the frozen transfer rate.

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