Preimplantation Genetic Screening of embryos using 24sure analysis

Concept Fertility Centre

12.2.13

Growing evidence suggests that a major factor in the failure to establish or maintain a pregnancy is when the cells in the embryo contain the wrong number of chromosomes, a condition termed aneuploidy. It has been known for some time that a significant number of human embryos have the wrong number of chromosomes (aneuploid). It is normal for a cell to contain 22 pairs of chromosomes plus the sex chromosomes, either XX for females or XY for males. Problems can arise when the embryo's cells contain too many or too few chromosomes. See back page for an expanded description.

A screening test called 24sure using array technology enables scientists to screen for aneuploidy in developing embryos and confirm that the correct number of all the chromosomes are present in each embryo.

What is 24sure?

24sure is a test that takes advantage of technology known as array comparative genomic hybridization (aCGH) and is a unique test because it makes thousands of independent measurements of the chromosomes at the molecular level.

24sure ensures a high degree of confidence may be placed in the results. The impact of 24sure on live birth rate is the subject of a number of ongoing studies. Preliminary studies have shown promising results and suggest increased birth rates in cases where chromosomally normal day 5 or 6 embryos are used. Larger trials are continuing.

Validation of 24sure aCGH

24sure aCGH was initially validated in 2009 in Cambridge UK and is now used in over 60 laboratories worldwide.

Recent validation studies show that 24Sure aCGH gives a 98% accuracy rate and results for 97% of the embryos tested. There have been numerous studies done to validate 24sure aCGH and these can be found on the website > www.24suretest.com <.

Who are eligible for PGS using 24sure aCGH?

- Those who are over 35 years of age
- Those who have a history of miscarriage (>2)
- Those who have had 3 or more IVF cycles without success
- Those who have a family history of aneuploidy

How is embryo screening with 24sure managed at Concept?

- Egg collection and ICSI
- Embryos frozen on day 5
- Embryo thaw and biopsy – removing 4-8 cells from each embryo on day 5 or 6 of development
- 24sure genetic analysis
- Embryos frozen on day 5 or 6 of development
- Frozen embryo transfer
- Once you have informed Concept that you would like to go ahead with testing please confirm your intention to start the test process by email to pgs@conceptfertility.com.au
  You will then be placed on the list for testing and be contacted with the test dates. You will have an appointment to receive results (5-10 days from biopsy). It is recommended not to start a frozen embryo transfer cycle until the results of the testing are known.

Considerations

- There is some increased risk of birth abnormalities in children born after ICSI (5% in naturally conceived children and 8% after ICSI).
- For the embryo biopsy and testing to take place the embryos need to be an expanded blastocyst on day 5 or 6.
- It is possible that the embryo might be damaged during the biopsy procedure although this is very rare (<1%) at Concept.
- It is possible that all the embryos will have the wrong number of chromosomes and therefore no embryos would be available for transfer. Research has shown that in couples where all their embryos were affected in the first cycle, 50% of these couples had an embryo suitable for transfer in their second cycle.
- Some embryos might not develop to day 5 and be suitable for biopsy or transfer even though they have the correct number of chromosomes. This is due to another developmental problem present in the embryo that is not associated with the number of chromosomes.
- There is a 6% chance an embryo may not survive the freezing process.
- If a low number of embryos (<5) are suitable for testing it might be possible to have another egg

collection procedure and then test both sets of embryos. Concept will need to apply to the Reproductive Technology Council for approval to undergo an egg collection procedure if three or more embryos are in storage.

- There is a cost for PGS (not included in IVF cycle related fees) and this is not covered by Medicare or private health insurance. Please see fee schedule (12.4.2).

Limitations of 24Sure

- The test results are 98% accurate. Part of the inaccuracy is because of mosaic embryos. That means the cells of the embryo are different and the biopsied cells have a different set of chromosomes to the remainder of the cells. In most mosaic embryos where some of the cells tested are abnormal other cells in the embryo can have a different abnormality. The difficulty arises when tested cells are normal and the cells remaining in the embryo are abnormal. This is a limitation of testing only a small number of cells. 24sure is able to detect some mosaic embryos.
- The results might be inconclusive for some embryos, and for some embryos a result is not possible, although these occurrences are rare (<3%).
- 24Sure cannot identify other abnormalities or birth defects that are not associated with the number of chromosomes and therefore doesn't guarantee a healthy pregnancy or birth.

Stages Involved In PGS

Embryo Biopsy –

Embryo biopsy procedure is performed by careful removal of a small number of trophecoderm cells that have herniated through the zona pellucida (outside shell) of an expanded blastocyst. The biopsy sample is then placed in a tube for testing and the embryo is cryopreserved.

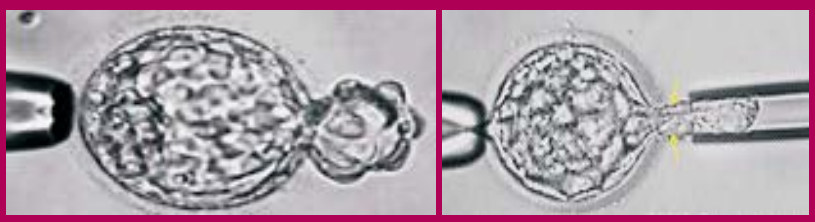
Genetic Analysis –

For PGS a technique known as array comparative genomic hybridization (aCGH) is used. This test is also known as 24sure.

Frozen Embryo transfer cycle –

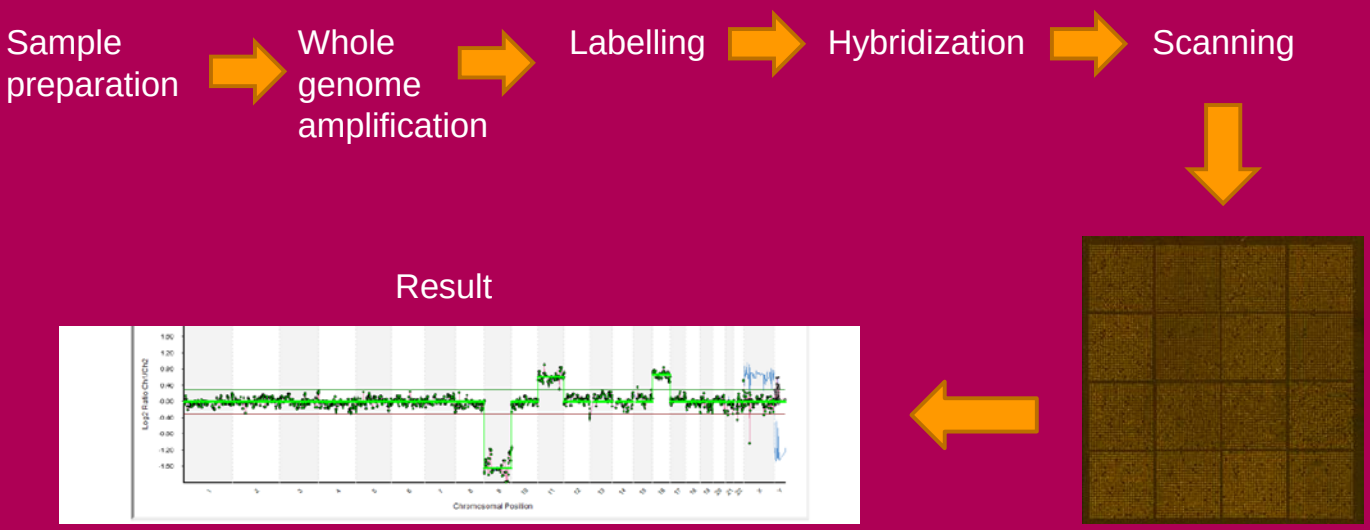
Unaffected embryo(s) can be transferred on day 5 or 6 in a frozen embryo transfer cycle. Excess normal embryos can remain frozen and stored for future use.

Embryo biopsy



Genetic Analysis

Genetic analysis for PGS is done using array comparative genomic hybridization (aCGH) with the 24Sure assay.



PGS Results

Figure 1

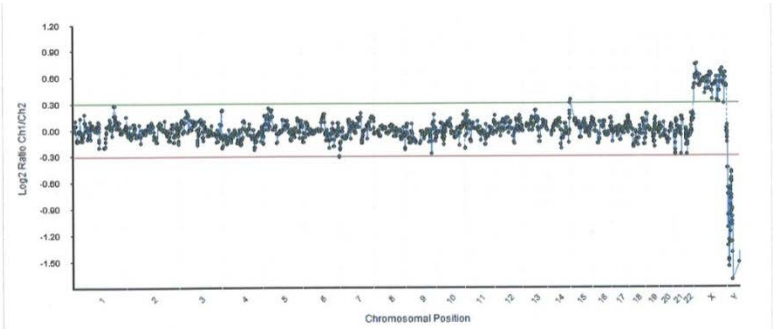


Figure 1 is an image of a 24sure analysis showing results from an embryo with the correct number of chromosomes. In this case there are two copies of each chromosome except the Y chromosome which is missing (image from Fishel et al J Fertiliz In Vitro 2011).

Figure 2

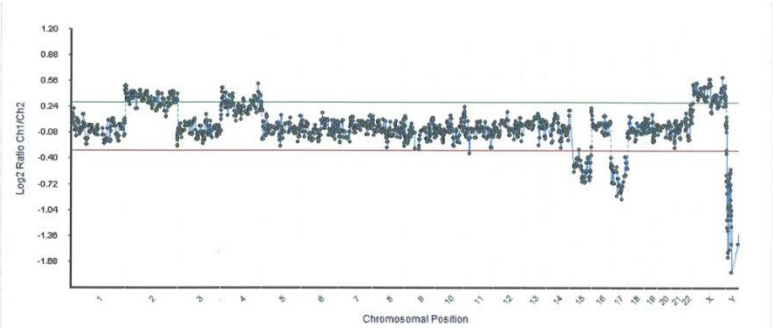


Figure 2 is an image of a 24sure analysis showing results from an embryo with extra chromosomes 2 and 4 and a 15 and 17 chromosome missing (image from Fishel et al J Fertiliz In Vitro 2011).

Genetics and chromosomes

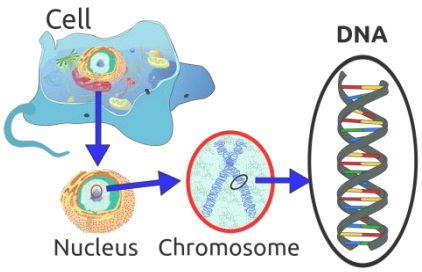
Our bodies are made up of millions of cells which each contain a complete copy of our individual genetic makeup (genes). The genes are tightly packaged together in the cells in the form of chromosomes. Each cell should contain 46 chromosomes (22 pairs and the two sex chromosomes). The chromosomes are numbered from 1-22 and the sex chromosomes are called X and Y. A female will have two X chromosomes and a male one X and one Y.

A chromosomal condition occurs when an individual is affected by a change in the number, size or structure of his or her chromosomes. These changes in the cells may result in problems in growth, development and functioning of the body systems.

There are two main types of chromosome changes that can occur – structural and numerical. Structural changes include chromosome translocations which occur when chromosomal material from two or more chromosomes are rearranged. These can also be detected using aCGH.

Human embryos have a high rate of chromosome imbalance (aneuploidy) and this is closely related to female age. The table below shows the frequency of normal embryos (euploid) tested on day 3 and 5 of development and female age. This provides a percentage estimation of the likely chance a woman of a particular age would have a normal embryo.

For more information please contact the Scientific Director at Concept on 9382 2388.



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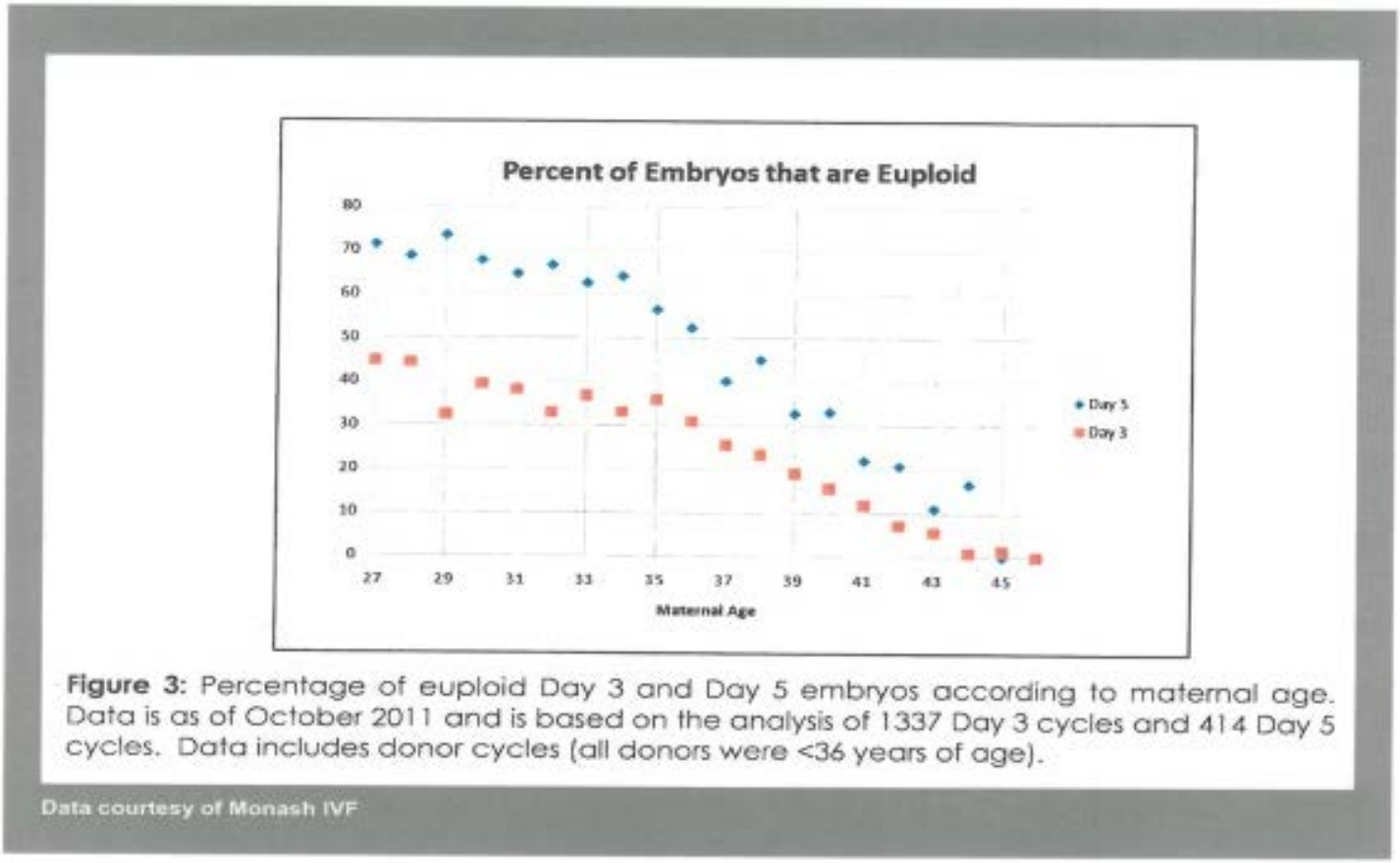

Figure 3: Percentage of euploid Day 3 and Day 5 embryos according to maternal age. Data is as of October 2011 and is based on the analysis of 1337 Day 3 cycles and 414 Day 5 cycles. Data includes donor cycles (all donors were <36 years of age).

Data courtesy of Monash IVF