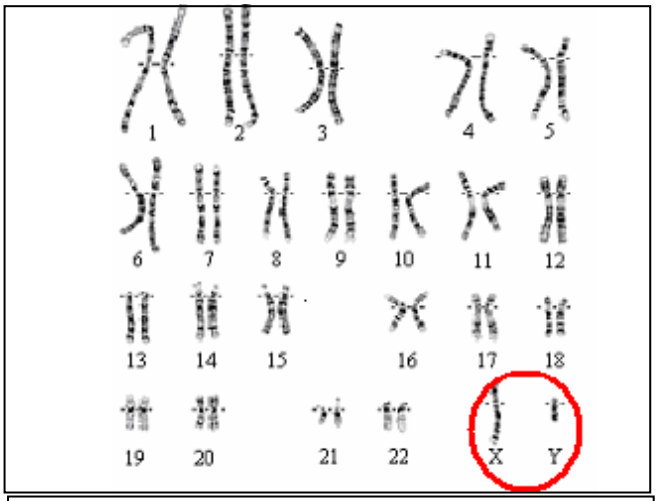
Patient Information

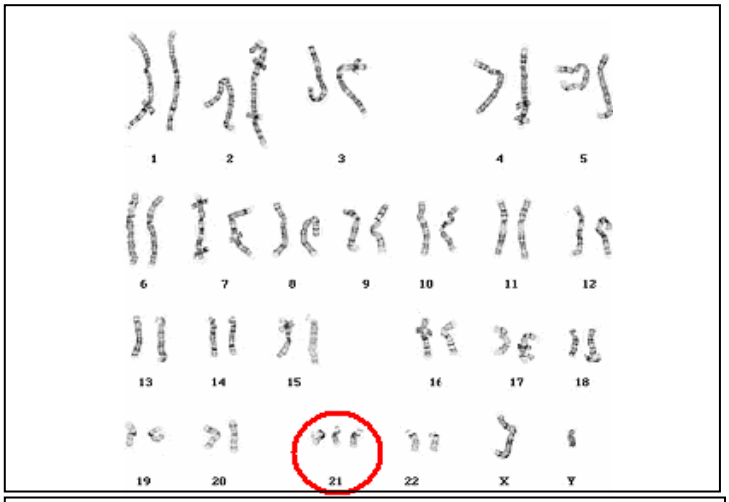
DONATING FROZEN EMBRYOS TO RESEARCH PROJECT R0188: to examine concordance and mosaicism in embryos

Background

IVF and natural conception are wasteful reproductive processes in terms of embryo survival. This is more apparent in humans than probably any other species. Approximately 70% of embryos produced – by either process – are lost before birth. The vast majority of embryos are lost within the first three months of pregnancy, and the majority of these even before implantation. A major cause of embryo loss, including miscarriage, is a chromosome anomaly (known as 'aneuploidy') arising in one or more of the 23 pairs of chromosomes. Chromosomes in all nucleated cells of the body, except the sperm or egg cells, exist in pairs; anomalies can exist if, for example, the whole pair is missing; if there is only a single chromosome or if there are three copies of the chromosome.

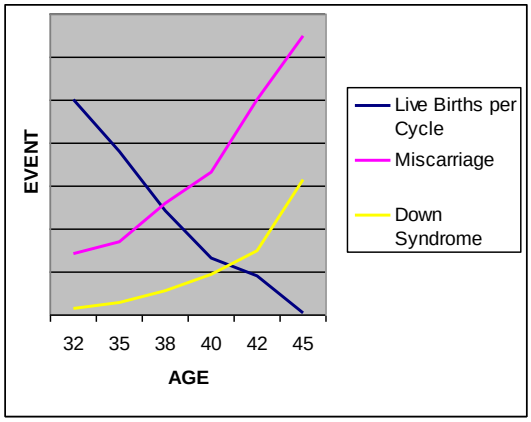


This is an example of a full set of chromosomes. The test to look at the chromosome number is called a **karyotype**. There are two of each chromosome from 1 to 22. As there is one X chromosome and one Y chromosome here, this karyotype represents a male.



This is an example of a karyotype of an individual with **Down Syndrome (Trisomy 21)**. You can see the two copies of each chromosome in pairs. However, if you look at chromosome 21 you will see that there are three copies (trisomy). The presence or absence of a whole or part of a chromosome is known as **aneuploidy**.

Some of these anomalies are compatible with full term delivery (such as three copies of chromosome 21 (known as Down syndrome) or three copies of chromosome 18 (Edward Syndrome). Others are not compatible with full term delivery and some anomalies cause the embryo to arrest its development before implantation.



The rate of aneuploidy in eggs increases with a woman's age. The most commonly known chromosome aneuploidy is Down Syndrome. This table shows that with advancing age a woman's risk of aneuploidy (Down Syndrome in particular) and chromosome-related miscarriage increases significantly, causing a major reduction in live birth rates.

Improving current practice of IVF requires an approach that would:

i) reduce embryo wastage
ii) improve pregnancy rates
iii) improve delivery rates by reducing miscarriage
iv) reduce the incidence of multiple births
v) maximise pregnancy rates with the transfer of only a single embryo.

This ultimate goal can be phrased as 'One Embryo-One Baby'!

What is PGS

Preimplantation Genetic Screening (PGS) is a complex technique for the detection of chromosomal imbalances, particularly any gains or losses of DNA in a sample of cells.

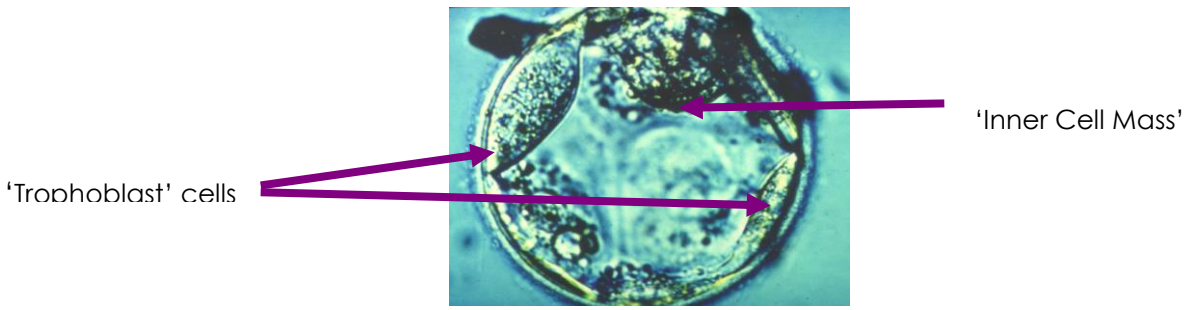
Why do we need to use embryos?

If an egg or sperm carries abnormal chromosomes, the cells of the embryo it creates will also be abnormal. However, if the egg and sperm are normal for its chromosomes, there is still a chance that some of the dividing cells themselves spontaneously develop abnormal chromosomes. Therefore by taking a cell from the embryo, or multiple cells at the blastocyst stage, we can examine chromosomes derived from the egg and the sperm and any chromosome errors that occur after fertilisation, thereby, getting a truer representation of the embryo.

Embryos donated for this research project will be thawed and cultured to day 5/6 (if frozen at an earlier stage of development) in preparation for embryo biopsy.

What is a 'Blastocyst'?

A blastocyst is the name given to the embryo five days post-fertilisation. Following fertilisation the fertilised egg (zygote) starts to divide, first into two cells, then three, four, five and so on – each cell dividing at its own rate. By day 4, when there are around 16 cells, a few of the cells gather towards the middle of the embryo. These cells start to progress slightly differently than the ones on the outside. By day 5 when there are approximately 25-60 cells the cells in the middle are all connected as a mass – known as the 'inner cell mass'(ICM); those on the outside are known as the 'trophoblast' cells. This is very important for the future development of the embryo once it implants in the womb. The inner cells only will become the baby; the trophoblast cells are now destined to become the placental tissue. Both cell types have come from the same egg and sperm, so if the egg or sperm has contributed any abnormal chromosomes that information is in the trophoblast cells. If we can take the cells from the trophoblast we can get this additional information about the embryo without having to biopsy the ICM or the embryo's actual cells.



Day 5 blastocyst

Aim of the research

Our aim is to compare the chromosomal content of two different areas of trophoblast cells and the isolated ICM from the corresponding blastocyst. A biopsy shall occur on day 5 or 6 and two areas of trophoblast cells will be biopsied (one close to the ICM and the other opposite it). The ICM will be isolated from the rest of the blastocyst and then all three samples will be prepared for PGS testing. We predict that the chromosomes in the cells of the ICM will be the same or similar to those from the trophoblasts.

How is this research regulated?

By law, all studies on human embryos must be approved and licensed by the Human Fertilisation and Embryology Authority (HFEA). Approval has been given for this study. The HFEA patient information sheet about embryo research is available for you at the unit or you can access it online at the HFEA website. In addition, all research projects have to be approved by the Local Ethics Committee.

Who is funding this research?

This research project is funded by CARE and Genesis Genetics Europe, which is the PGS testing laboratories used by CARE.

Where will this work be carried out?

The practical work will be carried out at CARE Nottingham, and embryos frozen at other CARE clinics may be transported to CARE Nottingham for the research to be carried out.

Will my confidentiality be protected?

Yes, the Human Fertilisation and Embryology (HFE) Act imposes strict requirements on patient confidentiality so any cells sent to the testing laboratory will be anonymously coded.

Will I receive any feedback from the research?

No feedback will be routinely given to individuals.

Important Regulatory Aspects

If you have consented to the use of your embryos in the research project you can still withdraw your consent to research at any time up to when the embryos are used in the research project. If you choose to do this, it will have no effect on you or your treatment if that is still on-going. If you wish to withdraw your consent please email alison.campbell@carefertility.com, or contact the unit at which you were treated and ask to communicate with the Laboratory Manager.
Your decision on whether or not to donate to the research project will have no influence on your ongoing fertility treatment, as only embryos considered unsuitable for use in treatment, or excess to treatment requirements, will be used in the research project. As explained in the Consent Form, this does mean you will not be able to gain any information relating to your particular embryo.
At the end of the research all embryos will be allowed to perish.
Please note that we encourage you to ask any questions that are on your mind at the time of signing the Consent Form or anytime thereafter. If you have any later questions you should contact the Laboratory Manager at the CARE clinic at which you had your treatment.

Glossary

Aneuploid (aneuploidy)	An abnormal chromosome profile in a cell
Blastocyst	The stage 5 – 6 days after fertilisation when the zygote has reached about 30 or more cells
Biopsy	The process to remove one or more cells
Chromosome	The part of the nucleus that carries the genetic information. One chromosome may carry over 1000 genes, and there are 23 pairs of chromosomes in the nucleus of a single cell
Embryo	The name given to the zygote once it divides into two cells, and continues cell division
Euploid	A normal chromosome profile
Gamete	The sperm or egg
Inner Cell Mass	A bundle of cells at one end of the blastocyst that together will eventually form the embryo after implantation
Nucleated Cells	The central part of almost all cells, which contains the chromosomes and genetic material
PGS	Preimplantation Genetics Screening– a technique used to analyse all the chromosomes within cells.
Trophoblast	The cells of the blastocyst that will not contribute to the embryo itself, only the placenta. Hence the precursor cells of the placental tissue