GENETIC SCREENING OF embryos

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In modern society where couples are opting to become pregnant at an advanced maternal age and many other couples are experiencing recurrent pregnancy losses and related fertility issues, techniques that test for genetic abnormalities in early embryos and foetuses are becoming valuable tools to increase the chances of successful and healthy pregnancies.

Preimplantation genetic testing (PGT), prenatal aneuploidy screening (PAS) and noninvasive prenatal testing (NIPT) are just a few services offered by Genesis Genetics to examine the genetic material of early-stage embryos and foetuses.

Genesis Genetics opened the doors to one of its newest laboratories based in SA, in August 2013 and has since been enjoying tremendous success in assisting the country’s top fertility and foetal assessment clinics in increasing the rate of successful pregnancies and the diagnoses of foetal abnormalities through the process of genetic testing using advanced molecular techniques.

Advances

Since the advent of genetic testing, science has taken a massive step forward. Genetic advances have afforded geneticists the remarkable opportunity to examine any individual’s genetic make-up and have even provided geneticists with the tools necessary to map a person’s entire ancestry.

Taking this process one step further, the concept of genetic screening of embryos now allows for the genetic profiling of embryos prior to their transfer and implantation into the uterus of a patient undergoing in vitro fertilisation (IVF). Through this process, geneticists can establish whether there are any genetic abnormalities associated with the embryo.

Further to this, geneticists are able to perform advanced molecular tests on foetuses, in pregnancies where genetic abnormality is suspected. These genetic abnormalities may include any extra or missing chromosomes or deletions or duplications of genetic material (DNA).

In IVF treatment, for example, these screening procedures can provide extremely important genetic information to fertility doctors, who have to establish which embryo(s) are of the best quality to transfer to their patient’s uterus. Thus, these new screening genetic processes can greatly increase the ratio of successful pregnancies and is a vital part of helping build healthy families.

Helping build healthy families is a sentiment that is shared by the Genesis Genetics family - particularly at their new South African Laboratory.

Genesis Genetics SA

Despite being new to SA, Genesis Genetics is a well-established global leader in PGT. One of its founders and CEO, Dr Mark Hughes, has played a leading role in pioneering PGT procedures. Genesis Genetics currently has over eight laboratories all over the world, from the USA to Brazil and even in Taiwan. Genesis Genetics SA, one of the latest additions to the Genesis Genetics family, opened just over a year ago in Johannesburg and offers PGT, PAS and NIPT to a variety of clients throughout the country.

“In order to remain competitive in the rapidly progressing medical field, fertility specialists, obstetricians, and gynaecologists are realising the immense importance and value that advanced molecular technologies offer to their practices in terms of the scope of healthcare services that they are able to provide to their patients,” said Dr Jayson Knezovich, Genesis Genetics SA’s Laboratory Director.

PGT

PGT is the term used to describe the testing of early stage embryos (under five days cl) for any genetic abnormalities prior to transfer to a patient’s uterus. This test is often offered as a complement to a patient’s IVF treatment.

Preimplantation genetic screening examines all 24 types of chromosomes of the embryo for any chromosomal abnormalities
Patients are typically referred for these tests because:

- They suffer from recurrent miscarriages
- The female partner is of advanced maternal age (>35 years old, when the risk of having a child with certain genetic abnormalities, such as Down’s Syndrome is greatly increased)
- There is a familial genetic disease/condition that they do not want to pass onto their children, such as sickle cell anaemia.

**Types of tests**

PGT consists of two different types of tests, namely preimplantation genetic screening (PGS) and PGD diagnosis (PGD).

PGS

PGS is a procedure that examines all 24 types of chromosomes (the 22 autosomes and the sex chromosomes X and Y) of the embryo for any chromosomal abnormalities. This test screens the material (DNA) and translocations (large structural rearrangements of the DNA). These chromosomal abnormalities will usually result in an unsuccessful pregnancy as the embryo will not be compatible with life or can manifest as a genetic condition in the child. PGS makes use of comparative genome hybridisation (CGH) microarrays to screen chromosomes and compares it to a known, genetically normal control using thousands of genetic markers across the genome. Genesis Genetics SA also offers translocation screening using their CGH microarrays, which offers a much higher resolution PGS test.

PGD

PGD is a test that is specifically designed to detect a known mutation, which is causing a familial genetic condition. Using over a decade of expertise, Genesis Genetics is able to design PGD tests for over 400 genetic conditions. As a diagnostic test, PGD makes use of technology that is designed to test a very specific mutation that is unique to a particular family. This test thereby enables fertility doctors to determine which embryos will carry or be affected with the inherited genetic disease. This genetic information helps fertility specialists to choose embryos unaffected by the condition to transfer to a patient’s uterus.

**PGT process**

IVF is a procedure that is becoming ever more popular for couples who experience difficulties conceiving naturally. This might be due to damaged or blocked fallopian tubes, severe endometriosis, severe male infertility, advanced age/decreased ovarian function and unexplained infertility. During IVF treatment the patient is stimulated to produce many eggs (oocytes).

The eggs are retrieved from the patient (or donor eggs are used) and fertilised using the partner or donor sperm in the IVF laboratory. The fertilised eggs are now embryos and start to grow in controlled conditions in the IVF clinic and undergo cellular division. Once these embryos are three or five days old, trained embryologists will biopsy each embryo.

During the biopsy, the embryologist removes a single or a few cells from the embryo. This biopsy does not impact on the development of the embryo. The biopsied cells are then sent to Genesis Genetics SA, where PGT is performed while the embryos continue to grow safely at the IVF clinic.

Once Genesis Genetics establishes which embryo samples are genetically normal or abnormal, they send a report to the referring IVF clinic.

The referring doctor then uses this information to decide which, and how many embryos to transfer to the patient’s uterus, where it will hopefully implant and give rise to a pregnancy. Transfer usually occurs when the embryo is five or six days old.

PGS has been shown to double the success rates of pregnancy because embryos that are genetically normal are more likely to be compatible with life. Thus, by transferring embryos back to the patient that are genetically normal, failure rates are significantly reduced.

**PAS**

Current methods for testing all 24 types of chromosomes on prenatal samples typically require cell culturing, which leads to lengthy turnaround times. Additionally, culturing prenatal samples is prone to cell culture failure. Alternatively, conventional methods that make use of molecular techniques only screen for a subset of chromosomes, including chromosomes 13, 18 and 21.

Using the same microarray technology that Genesis Genetics SA uses for PGS, they are able to screen all 24 types of chromosomes in a prenatal sample with PAS. This technique allows the geneticists to screen all of the chromosomes in the genome of a prenatal sample for any abnormal chromosome number (aneuploidies) or large genetic deletions or duplications. Much like PGS, this test screens the 22 autosomes and the two sex chromosomes. The tissues that Genesis Genetics SA is able to test include amniotic fluid, chorionic villus samples and products of conception.

This test is the first of its kind in SA, where the latest microarray technology is employed to rapidly and accurately screen prenatal samples for aneuploidies. Genesis Genetics has a turnaround time of three days with an accuracy of 99%.

**References available on request.**

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**Noninvasive prenatal testing (NIPT)**

The Genesis Serenity noninvasive prenatal test (NIPT) employs the latest technology from Illumina, one of the largest DNA sequencing companies in the world. This test uses the Verif® test to examine cell-free foetal DNA from a pregnant woman’s blood, in order to screen for aneuploidies of chromosomes 13, 18 and 21 in the baby’s genome.

The test can also screen for other conditions caused by missing and extra copies of the sex chromosomes (X and Y). Sex chromosome aneuploidies are conditions in which there is a change from the usual two copies of sex chromosomes in males (XY) or females (XX). All of these conditions may cause mental or physical defects with different levels of severity.

NIPT is usually offered to pregnant women who have a risk of a foetal aneuploidy. The Genesis Serenity test offers a new choice to women to have information about their pregnancy as accurately as possible from a simple blood draw, with no risk to their pregnancy.

This screening test may be an option to consider if there is a confirmed singleton or twin pregnancy of at least 10 weeks gestational age, and the patient meets any of the following criteria:

- They are of advanced maternal age (35 years or older (singleton pregnancy) or 32 years or older (twin pregnancy)) at time of delivery.
- They have an abnormal or positive serum screen.
- The ultrasound of the patient shows concerns or abnormalities with foetal growth and/or development.
- The patient has a personal or family history of aneuploidies of chromosomes 13, 18, 21, or the sex chromosomes. Although the Genesis Serenity NIPT is just one of many other screening tests, it does have many advantages. It provides more accurate information than calculating risk scores, which is often done in other genetic screening tests. This process is also noninvasive, as it makes use of a simple, single blood draw from the mother’s arm, and therefore poses no additional risk for complication (miscarriage) to the pregnancy.

**The New England Journal of Medicine (NEJM)** recently reported on the findings of the first NIPT randomised control clinical trial. The study showed how the Verif NIPT was used to screen 1914 pregnancies for trisomies.

In this group of patients, the Verif test successfully detected trisomy 13, 18 and 21 in all cases with confirmed trisomies. The authors of the article concluded: The significantly and substantively lower false positive rates with Verif screening than with standard screening, augurs well for pregnant women and their foetuses.'