New genetic sequencing methods mean quicker, cheaper, and accurate embryo screening

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Results from the first study of the clinical application of next generation DNA sequencing (NGS) in screening embryos for genetic disease prior to implantation in patients undergoing in-vitro fertilisation treatments show that it is an effective reliable method of selecting the best embryos to transfer, the annual conference of the European Society of Human Genetics will hear tomorrow (Sunday). Dr Francesco Fiorentino, from the GENOMA Molecular Genetics Laboratory, Rome, Italy, will say that his team's research has shown that NGS, a high throughput sequencing method, has the potential to revolutionise pre-implantation genetic screening (PGS). The technique can result in reduced cost, faster results, and accurate identification of good embryos resulting in more ongoing pregnancies, he will say.

The researchers undertook a prospective, double blind trial using two methods of embryo screening, NGS, and the older method array-comparative genomic hybridisation (Array-CGH) of 192 blastocysts, or early embryos, obtained from 55 consecutive clinical pre-implantation genetic screening (PGS) cycles. Array-CGH was the first technology to be widely available for the accurate analysis of chromosomal abnormalities in the embryo and is used extensively across the world for this purpose.

Fifty five patients with an average age of 40 years were enrolled; in 45 cases they were undertaking IVF because of advanced age and in ten

because of repeated IVF failures. Two different teams of researchers carried out biopsies and analysed the genetic make-up of the embryos at between five and six/seven days, depending on the speed of growth, and then measured the consistency of the diagnosis by comparing results from the two sequencing methods.

This comparison showed concordant results for 191 of the 192 embryos analysed. One embryo showed a false positive for three copies of chromosome 22 (trisomy 22) using the NGS technique. But analysis of this embryo also showed concordance between the two methods in detecting several other chromosomal abnormalities, and it would therefore have been ruled for transfer in any event. There were no other false negative diagnoses for chromosome abnormalities, and no inaccurate predictions of gender. NGS also showed itself to be as capable of identifying small, difficult to detect abnormalities.

"We found that results from the NGS and array-CGH diagnostic tests were highly concordant," Dr Fiorentino will say. "NGS allowed us to detect a number of different abnormalities in 4608 chromosomes with a very high degree of accuracy, and following the transfer of 50 healthy embryos in 46 women, 30 pregnancies continued."

These pregnancies were confirmed by the presence of a foetal sac and a heartbeat, and all have now completed at least 20 weeks of gestation.

PGS has been the subject of controversy over recent years. Initially hailed as an opportunity to improve clinical outcome in sub-fertile patients undergoing IVF, a number of studies later appeared to show that it might not help to identify and select chromosomally normal embryos for transfer based on its lack of benefit with respect to improving life birth rates.

"However, these studies used an older screening technique, fluorescent

in-situ hybridisation (FISH)," says Dr Fiorentino, "and we hypothesised that NGS might come up with more accurate results. The results of our study have proved this to be the case, and that NGS can improve clinical outcomes. We expect that the use of NGS technologies will increase as evidence of their utility becomes better-known.

"A further advantage of the technique is that it is quicker and cheaper, while remaining just as sensitive as other methods of screening. Our next step will be to participate in a large randomised controlled trial, the results of which will be critical for the acceptance of NGS-based pre-implantation embryo assessment into wider clinical practice."

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