First child born following embryo screening with new genome analysis technique

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The first birth has been achieved following the analysis of embryos using a new genome sequencing technique which promises to revolutionise embryo selection for IVF. The technique, which has never before been applied in the screening of embryos, is reported today at the annual meeting of ESHRE by Dr Dagan Wells of the NIHR Biomedical Research Centre at the University of Oxford, UK.

The analysis technique is known as "next generation sequencing", a powerful method capable of decoding entire genomes. Vast quantities of DNA data are produced from each sample tested, simultaneously revealing information on the inheritance of genetic disorders, chromosome abnormalities and mitochondrial mutations. Next generation sequencing (NGS) is already revolutionising many areas of genetic research and diagnostics, said Dr Wells, and, when applied to the assessment of embryos, will allow the concurrent analysis of serious inherited disorders and lethal chromosome abnormalities. "Next generation sequencing provides an unprecedented insight into the biology of embryos," said Dr Wells.

The identification of an embryo destined to implant in the uterus and form a pregnancy remains the holy grail of IVF. On average, only around 30% of embryos currently selected for transfer actually implant. The reason for this high failure rate is unknown, but the prime suspects are unidentified genetic or chromosomal defects. Several genetic screening methods have been introduced over the past decade, but all have been shown to have drawbacks (and have not realised their potential) when

tested in randomised clinical trials. This new NGS technique developed by Dr Wells and colleagues, however, seems to overcome the major drawbacks of current methods:

- Complete chromosome information can be produced revealing abnormalities often responsible for miscarriage
- Serious gene defects can be identified at the same time
- The analysis can be completed rapidly (around 16 hours), thus avoiding the need for embryo freezing while awaiting results
- The test could greatly reduce the costs of embryo screening, which is currently an expensive add-on to IVF.

The study described today was designed to test the accuracy and predictability of NGS in embryo selection. The validation was performed on multiple cells from cell-lines with known chromosome abnormalities, gene defects (cystic fibrosis) or mitochondrial DNA mutations.

Additionally, cells from 45 embryos, previously shown to be abnormal with another testing technique, were reanalysed by NGS in a blinded fashion. After high accuracy had been demonstrated, the method was applied clinically, with cells sampled from seven five-day-old embryos (blastocysts) produced by two couples undergoing IVF. The mothers were 35 and 39 years of age and one couple had a history of miscarriage.

NGS analysis in these two IVF patients identified three chromosomally healthy blastocysts in the first and two in the second; single embryo transfers based upon these results led to healthy pregnancies in both cases. The first pregnancy ended with the delivery of a healthy boy in June. Dr Wells, who led the international research team behind the study, said: "Many of the embryos produced during infertility treatments have no chance of becoming a baby because they carry lethal genetic abnormalities. Next generation sequencing improves our ability to detect

these abnormalities and helps us identify the embryos with the best chances of producing a viable pregnancy. Potentially, this should lead to improved IVF success rates and a lower risk of miscarriage.

"In the past few years, results from randomised clinical trials have suggested that most IVF patients would benefit from embryo chromosome screening, with some studies reporting a 50% boost in pregnancy rates. However, the costs of these genetic tests are relatively high, putting them beyond the reach of many patients. Next generation sequencing is a way which could make chromosome testing more widely available to a greater number of patients, improving access by cutting the costs. Our next step is a randomised clinical trial to reveal the true efficacy of this approach - and this will begin later this year."

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