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Mitochondrial DNA levels as a marker of embryo viability in IVF

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Despite the claims and counter-claims for new embryo assessment techniques introduced over the past two decades, the search for the holy grail of assisted reproduction - the key to the embryo destined to implant - continues. Genetic screening techniques so far have relied largely on the assessment of one component of the embryo's genetic constitution, the number of chromosomes in its cells. Studies dating back 20 years have shown beyond doubt that chromosomal abnormality is common in preimplantation embryos, and becomes even more common with increasing age. Chromosomal anomalies - or aneuploidy - are universally accepted as the main reason for miscarriage and the main cause of implantation failure

Methods that allow the screening of IVF embryos for aneuploidy are increasingly used during fertility treatments, helping doctors ensure that the embryos transferred have the correct number of chromosomes. However, even when a chromosomally normal embryo is transferred about one-third fail to produce a pregnancy.

Now, a new approach to embryo assessment described at this year's Annual Meeting of ESHRE may be able to shed light on why so many apparently healthy embryos are not viable. The approach is based on the quantification of mitochondrial DNA found in the outermost layer of cells in a five-day old embryo. The combination of chromosome analysis and mitochondrial assessment may now represent the most accurate and predictive measure of embryo viability with great potential for improving IVF outcome.

Following the presentation of these important results here in Helsinki, first author Dr Epida Fragouli from Reprogenetics UK and the University of Oxford's Nuffield Department of Obstetrics and Gynaecology in Oxford, UK, said the study "demonstrates that mitochondrial DNA levels are highly predictive of an embryo's implantation potential". Even embryos which are chromosomally normal and have a good morphological appearance under the microscope, she added, have virtually no ability to produce a baby if they have unusually high levels of mitochondrial DNA.

The evidence for mitochondrial DNA as an accurate marker of embryo viability came in a prospective study of 280 blastocysts (embryos cultured for five or six days) and tested to be chromosomally normal. The study was the first ever evaluation of the predictive power of mitochondrial DNA quantification with a prospective, blinded, non-selection design. This meant that the mitochondrial DNA levels of the blastocysts were not known at the time of transfer, so study results relied solely on a comparison of IVF outcome and mitochondrial DNA level, and were not subject to any bias.

Of the 111 single blastocyst transfers whose outcome was so far known, 78 (70%) led to ongoing pregnancies, and every single one of them (100%) had levels of mitochondrial DNA known to be normal. The remaining 33 blastocysts failed to implant, and eight of these (24%) had unusually high levels of mitochondrial DNA. Stratifying IVF outcome with mitochondrial DNA levels of low, normal and high produced an ongoing pregnancy rate of 76% (78/103) for morphologically good chromosomally-normal blastocysts with normal levels of mitochondrial DNA, but of 0% (0/8) pregnancy rate for the same type of blastocysts but with unusually high mitochondrial DNA levels. This difference, said Dr Fragouli, was highly statistically significant (P