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Clinical utilisation of a rapid low-pass whole genome sequencing technique for the diagnosis of aneuploidy in human embryos prior to implantation

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Abstract

Background The majority of human embryos created using in vitro fertilisation (IVF) techniques are aneuploid. Comprehensive chromosome screening methods, applicable to single cells biopsied from preimplantation embryos, allow reliable identification and transfer of euploid embryos. Recently, randomised trials using such methods have indicated that aneuploidy screening improves IVF success rates. However, the high cost of testing has restricted the availability of this potentially beneficial strategy. This study aimed to harness nextgeneration sequencing (NGS) technology, with the intention of lowering the costs of preimplantation aneuploidy screening.
Methods Embryo biopsy, whole genome amplification and semiconductor sequencing.
Results A rapid (<15 h) NGS protocol was developed, with consumable cost only two-thirds that of the most widely used method for embryo aneuploidy detection. Validation involved blinded analysis of 54 cells from cell lines or biopsies from human embryos. Sensitivity and specificity were 100%. The method was applied clinically, assisting in the selection of euploid embryos in two IVF cycles, producing healthy children in both cases.
The NGS approach was also able to reveal specified mutations in the nuclear or mitochondrial genomes in parallel with chromosome assessment. Interestingly, elevated mitochondrial DNA content was associated with aneuploidy ($p<0.05$), a finding suggestive of a link between mitochondria and chromosomal malsegregation.
Conclusions This study demonstrates that NGS provides highly accurate, low-cost diagnosis of aneuploidy in cells from human preimplantation embryos and is rapid enough to allow testing without embryo cryopreservation. The method described also has the potential to shed light on other aspects of embryo genetics of relevance to health and viability.

Full text:

http://jmg.bmj.com/content/51/8/553.abstract?maxtoshow=&HITS=10&hits=10&RESULTFORMAT=1&fulltext=innopsys&andorexactfulltext=and&searchid=1&FIRSTINDEX=0&sortspec=date&resourcetype=HWCIT