American Society for Reproductive Medicine 2017 Scientific Congress & Expo
October 28 to November 1, 2017 • San Antonio, TX, USA

Title

TARGETED NEXT GENERATION SEQUENCING (NGS) IDENTIFIES HIGHER PROPORTIONS OF MONOSOMIES IN THE LARGER CHROMOSOME GROUPS THAN qPCR

Authors:
C. Briton-Jones; L. Sekhon; J. A. Lee; R. Slifkin; M. Duke; A. B. Copperman

Affiliations:

1. Reproductive Medicine Associates of New York, 635 Madison Ave 10th Floor New York, New York, United States, 10022

2. Obstetrics, Gynecology and Reproductive Science, Icahn School of Medicine at Mount Sinai, Klingenstein Pavilion 1176 Fifth Avenue 9th Floor New York, New York, United States, 10029

Objective:
Targeted NGS has advantages as a preimplantation genetic testing (PGT) platform including: reduced cost, enhanced detection of partial chromosome deletions and duplications and greater potential for automation to reduce human error. Most NGS studies have compared trophoblast cells or aneuploid cell lines, diagnoses, to those obtained by existing PGT technologies. This study compared differences in the frequency of chromosome specific aneuploidies by NGS and quantitative polymerase chain reaction (qPCR).

Design:
Retrospective cohort analysis

Materials and Methods:
The study included patients undergoing autologous IVF cycles with embryonic aneuploidy screening by qPCR and NGS from January 2012 to February 2017. Donor oocyte IVF cycles and translocation carriers were excluded. Trophectoderm cells, obtained via blastocyst biopsy during culture day 5 to 7, underwent CCS. Proportions of embryos that showed aneuploidy for a specific chromosome were separated into the two CCS techniques (NGS or qPCR). Affected chromosomes were grouped according to size (A-C: large (chromosomes 1-12, X); D-G: small (chromosomes 13-22, Y) and centromere position, using standard karyotype criteria. Chi-square test was used to determine statistical significance where $P<0.05$.

Results:
A total of 8551 blastocysts from 1556 patients were analyzed using qPCR or NGS for detection of chromosomal aneuploidy (Table 1). Aneuploid embryos determined by qPCR had a 41.7% incidence of chromosomal loss or gain in the A to C group chromosomes as compared to 67.1%

aneuploid embryos determined by NGS (p< 0.00001). When comparing chromosome gains of aneuploidy, qPCR identified 23.5% errors in the A to C chromosomes as compared to 29.6% identified by NGS (p=0.016). When comparing chromosome losses in the A to C chromosome groups qPCR identified 18.1% of aneuploid embryos carried this type of error whereas NGS identified 37.5% (P<0.00001). qPCR identified 93.3% of the aneuploid embryos as having a loss or gain error in the smaller chromosome groups: D to G; compared to 93.6% by NGS (NS).

Conclusions:

This study demonstrates that in smaller chromosomes, NGS and qPCR provide similar aneuploidy detection rates. In larger chromosomes, however, NGS detected significantly more abnormalities than qPCR, particularly with regard to chromosomal monosomies. These findings demonstrate that the improved whole chromosome resolution obtained with NGS that allows for a more comprehensive evaluation of chromosome-specific gains and losses.

Support:

None.

Table 1: Proportion of aneuploid embryos and chromosomal specific aneuploidy by chromosome group.

	Patients	Embryos biopsied	Proportion aneuploid	Proportion of aneuploidy affecting groups A-C	Proportion of aneuploid gains affecting groups A-C	Proportion of aneuploid losses affecting groups A-C	Proportion of aneuploid affecting groups D-G	Proportion of aneuploid gains affecting groups D-G	Proportion of aneuploid losses affecting groups D-G
qPCR	1244	6751	37.15	41.7**	23.5*	18.2**	93.3	51.4	42.0
NGS	312	1800	34.94	67.1**	29.6*	37.5**	93.6	45.6	48.0

*P<0.05; **P<0.00001