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**Title:**

DOES THE NUMBER OF TROPHECTODERM CELLS ANALYZED BY TARGETED NEXT GENERATION SEQUENCING CORRELATE WITH THE INCIDENCE OF ANEUPLOID, MOSAIC OR INDETERMINATE RESULTS

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**Objective:**

Trophectoderm cells extruded from the expanding blastocyst provide meaningful genetic information regarding reproductive competence. The number of cells removed at biopsy may be a function of the number of cells present in a dividing blastocyst, and a surrogate marker for embryo quality. We hypothesized that the number of trophoctoderm cells identified in a biopsy sample could predict blastocyst quality and that the number of biopsied cells could be a marker of test performance. This study sought to evaluate whether the number of cells obtained at biopsy is correlated with the preimplantation testing (PGT) result.

**Design:**

Retrospective, observational study

**Materials and Methods:**

The study included women that underwent IVF with PGT from February 2016 to April 2017. Embryos were cultured to expanded blastocyst stage and underwent trophoctoderm biopsy on day 5 to day 6 of embryo development. A qualitative assessment of the number of trophoctoderm cells removed was made by the embryologist performing the biopsy. Aneuploidy screening by targeted NGS was performed. The odds of aneuploidy, mosaicism, limited amplification and



indeterminate results in association with the number of trophectoderm cells removed for biopsy was determined. ANOVA, Chi square, and linear and binary logistic regression were used for analysis.

### **Results:**

A total of 1799 blastocysts were biopsied for PGT, with a total of 3 to 10 trophectoderm cells removed. When stratified by the number of trophectoderm cells biopsied, the patients had significantly different mean ages ( $p=0.01$ ), with a trend toward more advanced mean age in the cohort with fewer trophectoderm cells biopsied (Table 1). However, maternal age was not significantly associated with the number of cells removed at biopsy ( $\beta = -0.00167$ ,  $p=0.8$ ).

The odds of aneuploidy increased significantly with advanced maternal age (OR 1.2 [95% CI 1.14-1.20],  $p<0.0001$ ). Controlling for age, the number of biopsied cells did not impact the odds of an embryo being detected as aneuploid (OR 0.97 [95% CI 0.89-1.07],  $p=0.5$ ), mosaic (OR 1.08 [95% CI 0.61-1.93],  $p=0.8$ ), having limited/failed amplification (OR 0.69 [95% CI 0.34-1.43],  $p=0.3$ ) or indeterminate results (OR 1.06 [95% CI 0.64-1.77],  $p=0.8$ ).

### **Conclusion:**

There was no significant correlation between the total number of biopsied trophectoderm cells and likelihood of detecting blastocyst aneuploidy. Furthermore, the ability of NGS to yield definitive results for aneuploidy screening was not hindered, even when as few as 3 trophectoderm cells were sampled. These results are reassuring regarding the performance of targeted NGS for PGT, as the number of trophectoderm cells obtained during biopsy may vary widely depending on the number of cells available for sampling in embryos of varying quality and developmental stage. With continued advancements to NGS technology, PGT may progress towards reliable single-cell DNA extraction and ploidy analysis.

### **Support:**

None



**Table 1:**

Patients demographics and PGT (targeted NGS for aneuploidy screening) results according to the number of trophectoderm cells removed at biopsy.

Number of cells biopsied	3	4	5	6	7	8	9	10	P Value
Age	37.6	38.8	35.8	35.5	36.1	35.9	33.3	36.6	0.0105
Embryos biopsied	8	22	547	848	108	243	3	8	N/A
Percent Aneuploid	87.5% (7/8)	86.4% (19/22)	49.2% (269/547)	47.5% (403/848)	62.0% (67/108)	52.3% (127/243)	0.0% (0/3)	12.5% (1/8)	NS
Limited Amplification	0.0% (0/8)	0.0% (0/22)	0.5% (3/547)	0.7% (6/848)	0.0% (0/108)	0.0% (0/243)	0.0% (0/3)	0.0% (0/8)	NS
Indeterminate Results	0.0% (0/8)	4.5% (1/22)	0.5% (3/547)	0.7% (6/848)	0.0% (0/108)	1.2% (3/243)	0.0% (0/3)	0.0% (0/8)	NS
Special Considerations	0.0% (0/8)	0.0% (0/22)	0.7% (4/547)	0.4% (3/848)	0.9% (1/108)	1.8% (2/108)	0.0% (0/3)	0.0% (0/8)	NS
No Result	0.0% (0/8)	0.0% (0/22)	0.7% (4/547)	1.5% (13/848)	0.0% (0/108)	0.9% (1/108)	0.0% (0/3)	0.0% (0/8)	NS