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Oral Presentation

Blastocysts with disproportionally high mtDNA copy number can result in healthy babies

Manuel Viotti[a,b]*, Christo Zouves[a,b], Alan Brake[b], Jack Tyndall[b], Andrea Victor[b,c], Darren Griffin[c], and Frank Barnes[a,b].

[a] Zouves Foundation for Reproductive Medicine, Foster City, California, USA

[b] Zouves Fertility Center, Foster City, California, USA

[c] School of Biosciences, University of Kent, Canterbury, United Kingdom

* presenting author.

Correspondence: manuel@zouvesfoundation.org

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Introduction

Mitochondrial DNA (mtDNA) copy number has been proposed as a biomarker of implantation in IVF embryos. Some studies suggest that blastocysts containing disproportionately elevated levels of mtDNA per cell always fail to implant, and blastocysts implanting successfully have lower mtDNA levels on average (Fragouli et al, 2015; Diez-Juan et al, 2015). Other studies do not report such a trend, including one from our group (Treff et al, 2017; Victor et al, 2017). An explanation for the conflicting reports could be that the method for quantitation of mtDNA copy number varies across studies. As a result, technical guidelines have been proposed to increase uniformity of mtDNA quantitation (Wells, 2017). Here, we adhere to those guidelines in analyzing mtDNA copy number in a large number of blastocysts used for transfer, to determine whether it is a valid predictor of implantation.

Materials & methods

We quantified mtDNA levels in surplus product of the PGT-A process from blastocysts used in IVF with known outcomes. In order to satisfy the suggested guidelines for mtDNA quantitation, we used qPCR measuring a locus in the mtDNA sequence and a multicopy locus in the nuclear

DNA sequence, and computed the ratio between the two values. All molecular material was fresh and devoid of degradation.

Results

In our hands, unlike in previous reports, blastocysts with extremely high mtDNA levels successfully implanted and led to healthy births. If using mtDNA copy number to deselect embryos, these samples would not have been chosen for transfer. In addition, analysis of >100 blastocysts showed a statistically insignificant difference between mtDNA levels in implanted versus non-implanted blastocysts.

Conclusions

These findings suggest that in a single-clinic setting, measurement of mtDNA copy number might not provide any advantage to embryo ranking, and might even lead to de-selection of blastocysts that result to healthy pregnancies. The validity of measurement of mtDNA copy number requires further investigation, given different findings in individual centers.

References

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