

AN INCREASED MITOCHONDRIAL DNA/NUCLEAR DNA RATIO IS PREDICTIVE OF A HIGHER IMPLANTATION POTENTIAL IN EUPLOID EMBRYOS.

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Abstract Body

Introduction: Mitochondria are essential cellular power generators and responsible for redox processes during preimplantation embryo development. Next generation sequencing (NGS) for preimplantation aneuploidy testing (PGT-A) provides mitochondrial-DNA (mtDNA) information simultaneously with nuclear-DNA (nDNA). There are conflicting reports using the mtDNA/nDNA ratio as a biomarker of embryo developmental potential. We aimed to assess the blastocyst trophectoderm (TE) mtDNA/nDNA ratio for predicting implantation in euploid embryos in a large cohort, and examine cofactors that may influence this ratio.

Methods: VeriSeq NGS was performed on 3,719 biopsied blastocysts (876 patients). Early implantation outcomes were available for 858 transferred embryos. mtDNA/nDNA ratio was calculated using quality filtered, unique reads, correcting for gender, chromosomal aberrations and mosaicism level. Differences in mtDNA/nDNA ratio were analyzed with ANOVA and t-testing. Sub-analyses were performed for ploidy status, static morphology grading (good/average/poor), Embryoscope™(ES) vs. conventional incubator culturing (CI)

Results: Euploid embryos (n=2214) had a significantly lower mtDNA/nDNA ratio compared with mosaic (n=662, p=0.000000015) and aneuploid embryos (n=843, p=0.0000068). Of 791 euploid embryos transferred, implanted embryos (pregnancies with gestational sac) (n=398) had a higher mtDNA/nDNA ratio vs. non-implanted embryos (n=393) (p= 0.0478). This ratio was no different in implanted (n=31) vs. non-implanted mosaic embryos (n=36) (p= 0.3). Static morphologic grading did not impact the mtDNA/nDNA ratio, when comparing embryos of good (n=604) to average (n=1298) (p=0.27); to poor morphology (n=1818) (p=0.47), and average to poor (p=0.66). For embryos cultured in an ES, but not in a CI, a higher mtDNA/nDNA ratio was observed in implanted average morphology (n=110) vs. non-implanted (n=100) embryos, (p= 0.003) and in poor morphology implanted (n=71) vs non-implanted embryos (n= 81), p=0.026, but not in good morphology embryos (implanted n=64 vs non-implanted n=57, p=0.26).

Conclusion: Overall, euploid embryos had a significantly lower mtDNA/nDNA ratio than mosaic or aneuploid embryos. Higher mtDNA/nDNA ratios predicted increased implantation among euploid embryos. In addition, sub-analysis indicated that higher mtDNA/nDNA ratios may be useful in selection of embryos for transfer when graded as average or poor, and when cultured in the ES. Further studies with larger sample size and pregnancy outcome data are needed to adequately assess the importance of mtDNA/nDNA ratio as a biomarker for implantation.