

## **600: Blastocysts with disproportionately high mitochondrial DNA copy number can result in healthy babies**

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### **Objective**

To confirm or refute previous claims that mitochondrial DNA (mtDNA) quantitation should be used to rank embryos for transfer in the clinic because blastocysts with high mtDNA copy number invariably fail to implant.

### **Design**

Guidelines have been proposed to increase technical uniformity of mtDNA quantitation across centers from blastocyst-stage biopsies (Wells, Fertil Steril, 2017). Here, we adhere to those guidelines in analyzing mtDNA copy number in 109 blastocysts used for transfer in a single-clinic setting, to determine whether it is a valid predictor of implantation and birth.

### **Materials and Methods**

Levels of mtDNA were quantified in surplus product of the PGT-A process from blastocysts used in IVF with known outcomes. 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. Statistical comparison between implanted and not implanted groups was performed with a two-tailed unpaired t test.

### **Results**

Blastocysts with extremely high mtDNA levels successfully implanted and led to births. Clinical follow-up of five babies with highest mtDNA levels out of the 109 analyzed blastocysts indicated they were healthy at birth and normal for a panel of 63 screened conditions, including various metabolic disorders. If using mtDNA copy number to deselect embryos, these samples would not have been chosen for transfer, precluding the birth of five healthy babies. In addition, compiled analysis of the 109 blastocysts showed a statistically insignificant difference between mtDNA levels in implanted versus non-implanted blastocysts (average implanted=0.00617, stdev=0.00447, n=55; average not implanted=0.00528, stdev=0.00305, n=54; P=0.231, ns).

### **Conclusions**

The measurement of mtDNA copy number at the blastocyst stage might not provide any advantage to embryo ranking, and could lead to de-selection of blastocysts that result in healthy pregnancies and births. We conclude that the practice of mtDNA quantitation requires further investigation and validation, and consider the commercial push to implement this test in the clinic premature.

### **Support**

None.

### **Disclosure**

None.