

### INTRODUCTION

Chromosomal abnormalities are considered to be an important cause of implantation failure<sup>1</sup>. However, previous reports show that embryos consisting of a mixture of chromosomally normal and abnormal cells, also called mosaic embryos, can lead to healthy live births<sup>2</sup>. Still, the impact of abnormal cells on embryonic development remains unclear. Recent work on mouse embryos demonstrated that chromosomally abnormal cells are eliminated by apoptosis in the inner cell mass (ICM), whereas they show proliferative defects in the trophectoderm (TE)<sup>3</sup>. **We therefore hypothesize that chromosomally abnormal cells impact on expansion of the TE.**

### MATERIAL & METHODS

#### Blastocyst surface measurements

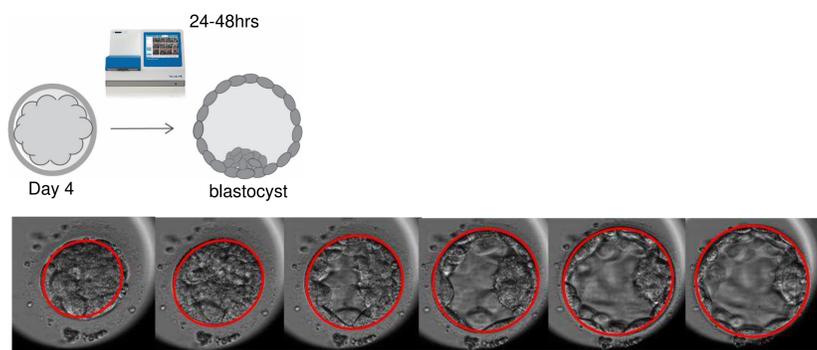


Fig 1. Time-lapse images of a human embryo during development from Day 4 post fertilization to Day 5.

Cryopreserved human surplus IVF embryos were thawed and cultured in the EmbryoScope time-lapse incubator, until blastocyst development. During the embryo culture, blastocyst surface measurements were taken every hour, starting at the blastocoel formation until the moment of the biopsy.

#### Genetic analysis of ICM and TE

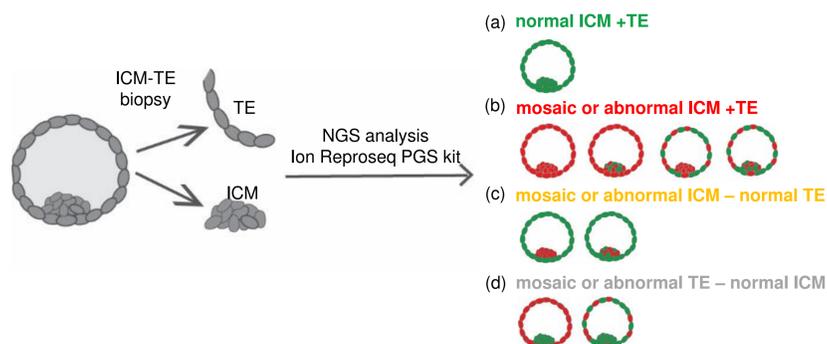


Fig 2. Schematic representation of embryo biopsy and analysis.

At the blastocyst stage, a TE biopsy was performed, the ICM was collected separately and both were chromosomally analyzed with the Ion ReproSeq PGS kit (ThermoFisher Scientific, MA, USA). In total, 45 embryos were analysed. According to the chromosomal constitution of the ICM and TE, the embryos were categorized into four groups: a) normal ICM+TE, b) mosaic or abnormal ICM+TE, c) mosaic or abnormal ICM - normal TE, d) mosaic or abnormal TE - normal ICM.

### REFERENCES

- McCoy RC, *Trends Genet.* 2017;33(7):448-463.
- Greco E, *N Engl J Med* 2015;373:2089-2090
- Bolton H., *Nat Commun* 7 2016;11165

### CONCLUSION

- We found a low blastocyst expansion rate to be indicative of the presence of chromosomally abnormal cells in both ICM and TE.
- The blastocyst expansion rate may help identifying embryos at risk for aneuploidy.
- A low blastocyst expansion rate may identify embryos with solely an affected ICM that have an increased risk of a false negative diagnosis when undergoing PGT-A.

### RESULTS

#### Growth graphs of each embryo

The blastocyst surface measurements were plotted against time (hrs) of culture resulting in growth graphs. From these the slope of the graph was determined, corresponding to the blastocyst expansion rate.

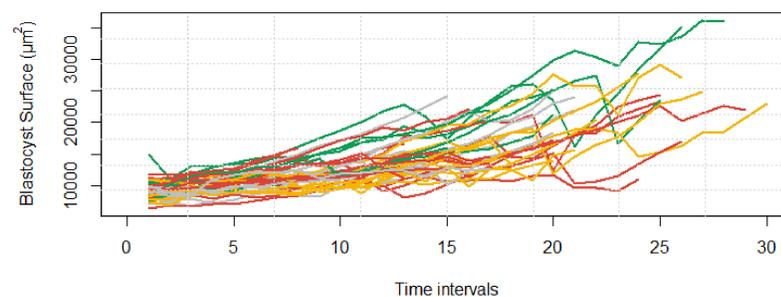


Fig 3. The blastocyst surface measurements of each embryo per hour. The four embryo categories are represented in a different colour; (a)-green, (b)-red, (c)-yellow, (d)-grey.

#### Blastocyst expansion rates correlate to the chromosomal constitution

The chromosomal constitution of the embryos was correlated to the observed blastocyst expansion rate. A statistically significant reduced expansion rate compared to the normal ICM+TE category, was observed in embryos with mosaic or abnormal ICM+TE and in embryos with mosaic or abnormal ICM - normal TE.

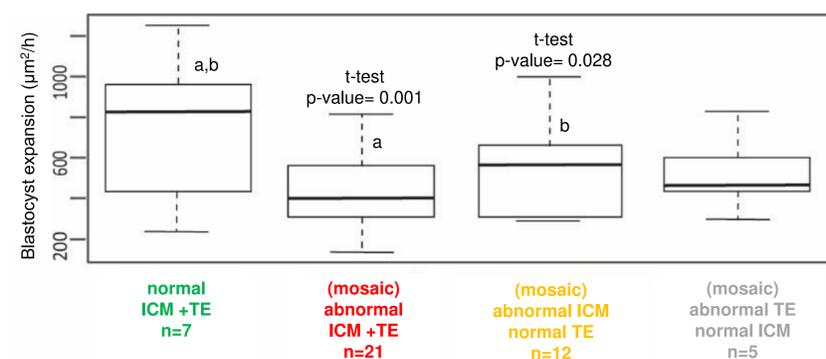


Fig 4. The blastocyst expansion rate of each embryo category. The box whiskers show the range observed, whereas the boxes indicate 25th and 75th percentiles. The horizontal line represents the median value. The significant different average blastocyst expansion rate of normal ICM+TE embryos towards (mosaic) abnormal ICM+TE (a) embryos and embryos with (mosaic) abnormal ICM - normal TE (b) are indicated in the boxplot ( $P < 0.05$ ).

### CONTACT

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