

Abstract Details

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★ Abstract title:

Comprehensive comparison of trophoctoderm (TE) and inner cell mass (ICM) by next generation sequencing (NGS)

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Study question:

Does the chromosomal information of trophoctoderm (TE) accurately predict the chromosomal information of the inner cell mass (ICM)?

Summary answer:

The observed discordance rate between TE and ICM was 15.9%. Hence, further exploration on the implication of mosaicism due to mitotic errors is mandatory.

What is known already:

The most important cause for implantation failure is chromosomal imbalance in the embryo. Identification of a chromosomally normal embryo is possible due to current techniques available; however, mosaicism can complicate interpretation of the result. Whereas meiotic errors of the oocyte result in uniform aneuploidies, errors occurring during the first three mitotic division of the embryo might lead to mosaicism. TE biopsy is commonly used to infer the chromosomal status of the ICM, hence in case of mosaicism, TE biopsy might not represent the correct chromosomal status of the ICM and could therefore lead to a misdiagnosis of embryo's chromosomal status.

Study design, size, duration:

Observational, blinded study, including 88 embryos, that underwent PGS prior embryo transfer, between August 2016 and January 2017. NGS technique used to compare the chromosomal status of the trophoctoderm and the inner cell mass in blastocysts on embryos that were not selected for transfer (including surplus euploid embryos that could not be cryopreserved according to the UAE law).

Participants/materials, setting, methods:

Infertile couples with normal karyotype undergoing PGS with fresh oocytes, female partner with age 18 to 45 years and a body mass index of 19 to 30. Only expanded blastocyst with distinguishable ICM were biopsied. The genetic laboratory was blinded regarding the identity of the couple and the origin of the sample.

ICM biopsy was performed as described in the validated procedure by Capalbo et al. 2013.

The patients were counseled and consents were obtained.

Main results and the role of chance:

Out of the 88 embryos, in which trophoctoderm and ICM biopsy could be performed, 14 embryos (14/88 = 15.9%) had a discrepant chromosomal status between ICM and trophoctoderm.

In depth analysis of the embryos with discordant findings of trophoctoderm and ICM, in 4 embryos (4/14 = 28.57%; 4/88 = 4.54%) ICM revealed an euploid finding and trophoctoderm an aneuploid finding (= false-positive for trophoctoderm biopsy). In 3 embryos (3/14 = 21.42%; 3/88 = 3.41%), ICM reported an aneuploid finding and trophoctoderm an euploid finding (= false-negative of trophoctoderm biopsy). Therefore in total 7 discrepancies (7/14 = 50%; 7/88 = 7.95%) regarding the embryo diagnosis (euploid / aneuploid; aneuploid / euploid) for whole chromosome analysis. The other 7 embryos (7/14 = 50%; 7/88 = 7.95%) had different chromosomal abnormalities in ICM and trophoctoderm.

Limitations, reasons for caution:

To thoroughly identify the exact rate of mosaicism, more embryos should be included in future studies.

Moreover, the well known methodological artefacts linked to the whole-genome amplification, warrant careful interpretation of the current findings.

Wider implications of the findings:

Mosaicism in the embryo results from mitotic errors during the first cleavage divisions and different proportions of the embryo can be affected. Our results of false-positive TE biopsy question the accuracy of aneuploidy results from TE biopsy in regards of being representative for the whole embryo.

Trial registration number:

Not applicable

Keywords:

Embryo biopsy

Mosaicism

NGS

ICM

TE