Optimization of a non-invasive PGT-A program: rescue of non-informative samples

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Introduction:

The analysis of the embryonic cell-free DNA (cfDNA) released by the blastocysts during their development can be used as a non-invasive method of preimplantation genetic testing for aneuploidies (niPGT-A). In a small percentage of samples, after an initial analysis, it is not possible to obtain a result, given the low concentration of the DNA released or its poor quality.

The objective of this study is to evaluate a rescue strategy applicable to these cases.

Material and methods:

The study included 35 embryos analyzed using niPGT-A (EMBRACE) in the period from April 2021 to August 2024. They were reported as "no DNA detected" or "Non-informative" due to the low concentration or quality of cfDNA, respectively, present in the drop of media where the embryos were cultured. The blastocysts, all day 6, were devitrified, washed and cultured for 8 hours. The culture medium was then aspirated and analyzed by NGS, and the embryos were re-vitrified (Figure 1).

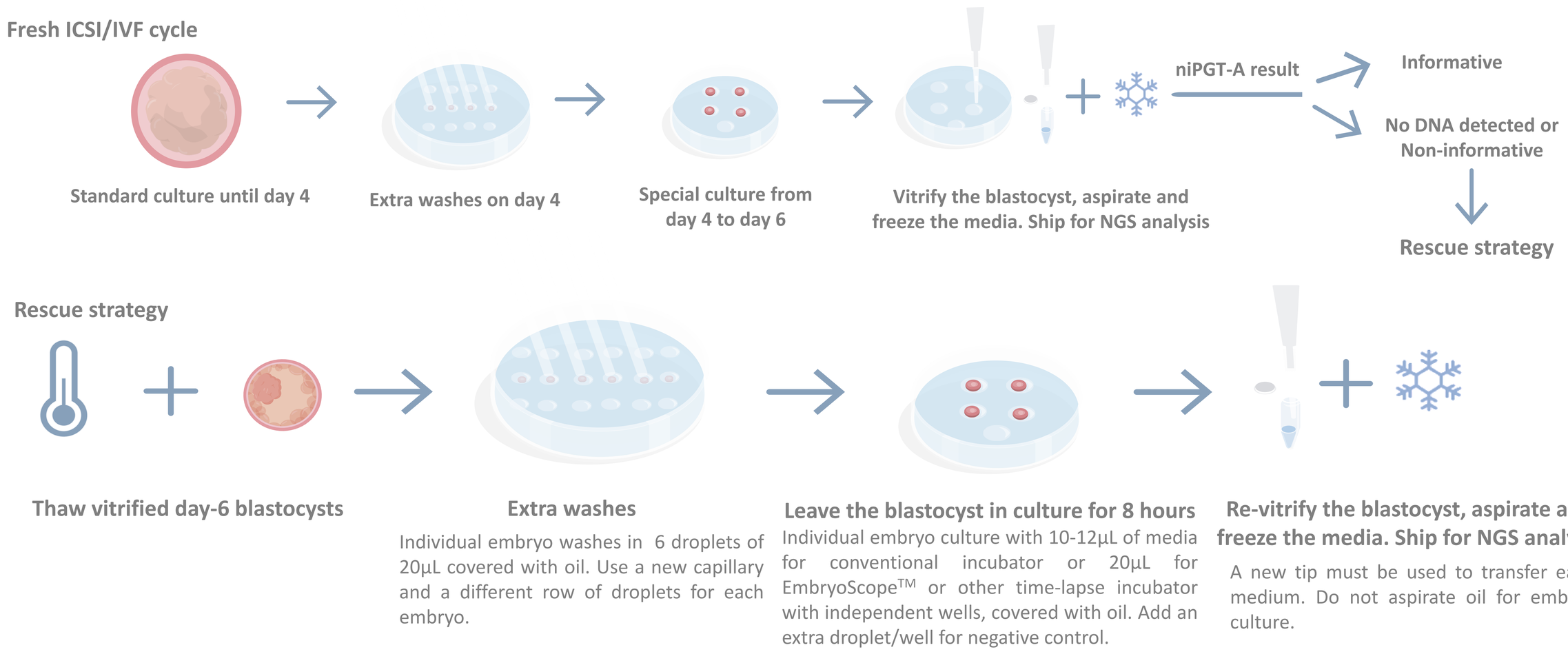

Figure 1. Scheme showing the niPGT-A embryo culture worflow as well as the rescue strategy to apply in case of an initial inconclusive result.

Results:

From the 35 blastocysts analyzed, 12 were initially reported as **"no DNA detected"** (mean age 38.5 ± 3.9). In 8 of them, an informative result was obtained on the second analysis: one of the blastocysts was considered euploid and the other 7 aneuploid, mostly showing one whole chromosome aneuploidy (Figure 2). **The rescue rate was 66.7%.**

The other 23 embryos were initially reported as **"Non-informative"** (mean age 36.5 ± 3.8). After reanalyzing them, informative results were obtained in 22: 8 were considered euploid and 14 aneuploid (7 of them with two whole chromosome aneuploidies). **The rescue rate was 95.7%.**

The overall rescue rate was 85.7% (30/35).

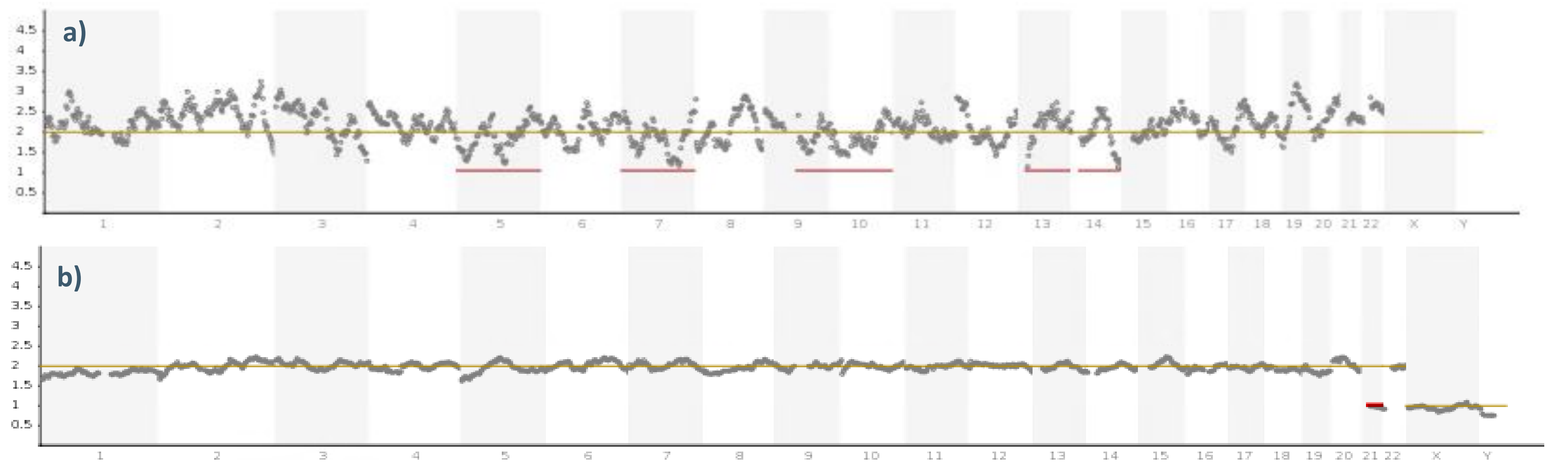

Figure 2. NGS profile showing how a sample considered as no DNA detected on the first niPGT-A analysis (a) is rescued after applying this strategy (b; aneuploid result, monosomy 21).

Conclusions:

The analysis of a second sample of culture medium in devitrified day 6 blastocysts allows the rescue of "Non-informative" samples or with "no DNA detected" previously analyzed by niPGT-A. This strategy has shown good results in niPGT-A and could also be applied to vitrified blastocysts with a previous non-informative PGT-A result. PGT-A and niPGT-A samples with inconclusive results due to contamination could also benefit from this approach.