



# Great Challenges Remain for niPGT-A Reliability

## *Restam grandes desafios para a confiabilidade do niPGT-A*

Bruno Ramalho de Carvalho<sup>1</sup>

<sup>1</sup>Bruno Ramalho Reprodução Humana, Brasília, DF, Brazil

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Address for correspondence Bruno Ramalho de Carvalho, Bruno Ramalho Reprodução Humana, SGAS 614, Conjunto C, Sala 177, 70200-740, Edifício VITRIUM - Centro Médico Inteligente, Asa Sul, Brasília, Distrito Federal, Brazil (e-mail: ramalho.b@gmail.com).

In the case report *First Baby Born in Brazil after Simultaneous Diagnosis through Non-Invasive and Conventional PGT-A* (Rev Bras Ginecol Obstet. 2021;43[11]), Kulmann et al.<sup>1</sup> present noninvasive preimplantation genetic test for aneuploidies (niPGT-A) as an alternative to conventional PGT-A. Those who defend the new technology assume that the biopsy of the trophoctoderm could affect embryo health and its implantation potential. Also, the proposed technique assumes that the cell-free DNA found in the spent culture media (SCM) represents the genetic status of the embryo. However, as highlighted in their *Introduction*, the concordance rates between trophoctoderm and SCM samples have been reported to greatly vary among studies, from insufficient ~ 30% (Vera-Rodriguez et al., 2018)<sup>2</sup> to amazing ~ 94% (Huang et al., 2019).<sup>3</sup> A critical look at this discrepancy leads the observer to realize that a lot of progress needs to be made before introducing that technique into the routine of the reproductive clinic.

Two studies by Rubio et al. (2019, 2020)<sup>4,5</sup> seem to be the pillars of this case report. The second study (Rubio et al., 2020)<sup>5</sup> is really interesting, since it included 1,301 human blastocysts, with promising concordance rates demonstrated. But uncertainties on the need to extend embryo culture to days 6 and 7, and the theoretical loss on reproductive potential of such blastocysts compared to day-5 ones are still concerning. Even with low-quality evidence, some studies suggest better clinical pregnancy and live birth rates in favor of day 5 blastocysts.<sup>6–11</sup>

Considering the expectation of presenting an accurate test, it seems intriguing to find out that total concordance between conventional and niPGT-A occurred only for 3/7 blastocysts in the presented case. In real life, partial concordance is a non-encouraging result, and I would dare to say that it is as inutile as a total discordance. Of note, other recent studies present frustrating concordance rates for autosomes or sex chromosomes between trophoctoderm or inner cell mass, and SCM analyses.<sup>12,13</sup>

Finally, it is important to highlight the optimization of culture conditions, SCM retrieval, DNA isolation, and amplification protocols as great challenges for niPGT-A reliability. To date, we must be concerned about the theoretical high risk of maternal contamination.<sup>14,15</sup> Fortunately, the authors indicate that niPGT-A is not ready to replace conventional technique in routine and that further studies are needed to lead science in the best direction.

### Conflict of Interests

The author has no conflict of interests to declare.

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