embrace

Embryo Analysis
of Culture Environment

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Culture time to optimize embryo cell-free DNA analysis for frozen-thawed blastocysts undergoing noninvasive preimplantation genetic testing for aneuploidy

Objective:

To identify the optimal time in culture needed to perform niPGT-A for frozen blastocysts, with or without previous TE biopsy.

Scan the paper

Experimental Design:

- Prospective, observational study.
- 135 donated frozen blastocysts, generated using standard intracytoplasmic sperm injection or conventional insemination, with and without previous PGT-A, from women aged 29–42 years were included.
- Blastocysts were divided in three groups and cultured according to our specific EMBRACE protocol, in either conventional or Time-lapse incubators:
  - Day-5 blastocysts cultured for 8 hours (Day-5 Short group, N=42);
  - Day-5 blastocysts cultured for 24 hours (Day-5 Long group, N=50);
  - Day-6 blastocysts cultured for 8 hours (Day-6 Short group, N=43).
- Media and whole blastocysts were analyzed, and the results were compared.

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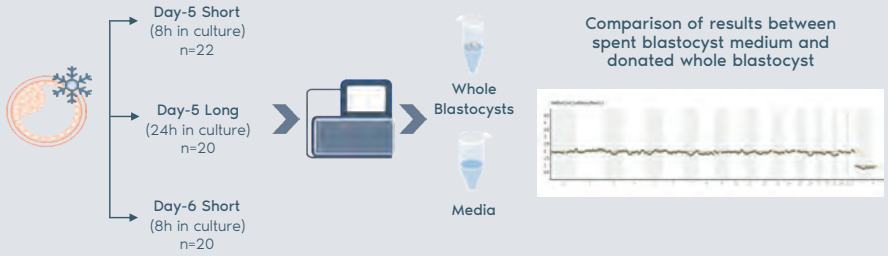
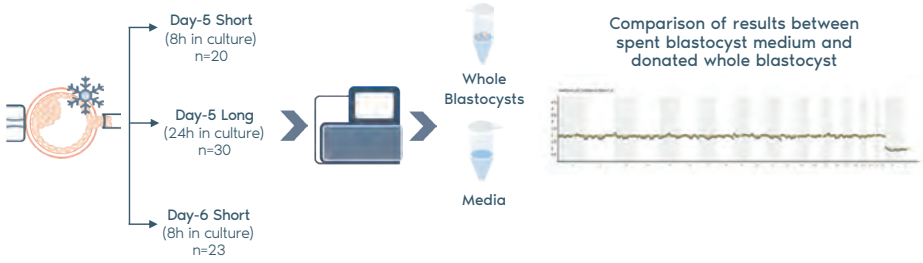
Non-PGT-A cycles
n=62



PGT-A cycles
n=73



Ardestani G, Banti B, García-Pascual CM, Navarro-Sánchez L, Zyl EV, Castellón JA, Simón C, Sakkas D, Rubio C
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Results:

Non-PGT-A cycles			
	Day-5 Short	Day-5 Long	Day-6 Short
Number of samples (N)	22	20	20
Informative spent media, n/N (%)	13/22 (59.1)	20/20 (100)	19/20 (95)
Informative whole blastocysts, n/N (%)	22/22 (100)	20/20 (100)	20/20 (100)
Informative media-whole blastocyst pair, n/N (%)	13/22 (59.1)	20/20 (100)	19/20 (95)
Concordance, n/N (%)	11/13 (84.6)	17/20 (85)	18/19 (94.7)

PGT-A cycles			
	Day-5 Short	Day-5 Long	Day-6 Short
Number of samples (N)	20	30	23
Informative spent media, n/N (%)	8/20 (40)	29/30 (96.6)	21/23 (91.3)
Informative whole blastocysts, n/N (%)	20/20 (100)	28/30 (93.3)	22/23 (95.7)
Informative media-whole blastocyst pair, n/N (%)	8/20 (40)	27/30 (90)	20/23 (87)
Concordance, n/N (%)	8/8 (100)	27/27 (100)	18/20 (90)

Informativity rates vs time in culture:

- Significantly lower informativity rates in Day-5 Short culture for both non-biopsied **(59.1%)** and biopsied **(40%)** compared to Day-5 Long and Day-6 Short groups.

Concordance rates vs time in culture:

- **No significant differences in concordance rates** comparing non-biopsied and biopsied embryos between the three groups.

Informativity and concordance rates vs. embryo quality before vitrification:

- All blastocysts were classified as good quality (ICM/TE grades were A or B) according to the Gardner scoring system. Expansion degree ranged between 3-6.
- The expansion degree did not have an effect on informativity and concordance rates.

Main Conclusions:

Non-invasive Preimplantation Genetic Testing for Aneuploidy (niPGT-A) can be effectively applied to frozen-thawed blastocysts, demonstrating informativity and concordance rates exceeding 90%.

The **key determinant for achieving high informativity rates is the duration of culture relative to the original vitrification day.** Specifically, a culture period of at least 24 hours for day-5 embryos and a minimum of 8 hours for day-6 embryos is required to obtain sufficient cell-free DNA (cfDNA) in the spent culture media for accurate analysis.

Prior embryo manipulation such as assisted hatching or previous biopsy do not impact cfDNA detection and informativity rates. There is no difference in informativity or concordance outcomes between frozen or fresh blastocysts, nor between different protocols involving various media volumes.

The use of previously frozen-thawed blastocysts, combined with additional washing steps, aids in removing contaminating cumulus cells.

We propose adopting our frozen-thawed blastocyst EMBRACE approach for re-analysis of no-result PGT-A blastocysts, and testing of previously vitrified non-PGT-A blastocysts.

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