STEM CELL-DERIVED BLASTOIDS AS BLASTOCYST BIOPSY TRAINING TOOLS IN THE IVF LABORATORY.

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Background
Proper training and development of embryologists in ART laboratories is crucial to a successful IVF program. Quality control and quality improvement exercises are required by many internal and external regulatory organizations. Most laboratories struggle to obtain donated or discarded materials for emerging embryologists to train with. In the quickly changing political and legal climate of today, these donated or discarded embryos also bear potential ethical concerns.

Objective
Stem cell-derived human blastoids have recently emerged as a new tool in modeling human development. Here, we begin to explore the potential to use stem cell derived blastoids as tools for embryologist training and quality control in the IVF laboratory.

Materials and Methods:
Human blastoids were created from naïve pluripotent stem cells based on an established protocol [1]. Good quality blastoids with at least 150 μm diameter (similar in size to a human blastocyst graded stages 3-6), a blastocoel cavity occupying greater than half of the embryo, and approximately 10-20% of the blastoid displaying well organized ICM-like cells within the blastocoel were selected for the experiment. Blastoids were subjected to either vitrification and warming or trophectoderm biopsy performed by trained embryologists (n=104). Vitrification and warming procedures were performed following the Kitazato protocol using in house medium. Biopsy procedures were performed on an Olympus inverted microscope using a Hamilton Thorne laser. Either a standard 3-6 cell sample with minimal pulses of the laser was taken (n=10) or blastoids were subjected to a traumatic biopsy (to simulate a novice or in-training embryologist); with greater than 10 cells being taken and a greater number of laser pulses at a higher power (n=10). All blastoids were recovered in culture medium for 2-3 hours to assess survival and re-expansion.

Result(s):
A total of 104 blastoids were vitrified and warmed, with 99.0% survival (103 out of 104). Most blastoids (91 out of 104, 87.5%) showed at least 25% re-expansion of the blastocoel cavity during the recovery period. Twenty blastoids were biopsied, all 20 survived biopsy, and all were of acceptable quality to vitrify after recovery. Blastoids were visually and technically similar to human embryos during the vitrification, warming, and biopsy procedures. Blastoids in the standard biopsy group had a slightly higher tendency to re-expand (60%) than those in the traumatic biopsy group (40%).

Conclusion(s):
This small preliminary study shows that stem cell-derived blastoids can successfully survive standard ART procedures including vitrification, warming, and trophectoderm biopsy while

mirroring typical behavior of human blastocysts. In the biopsy group, blastoids reacted negatively to an improper, traumatic biopsy, suggesting that laboratories could use them as a marker of quantifiable success (or failure) in training exercises. Stem cell derived blastoids show great promise as tools for embryologist training and quality control practices in the IVF laboratory.

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References:

1. Yu L, et al., *Large-scale production of human blastoids amenable to modeling blastocyst development and maternal-fetal cross talk*. Cell Stem Cell. 2023 Sep 7;30(9):1246-1261.e9. PMID: 37683605.