Genes & Diseases (2016) 3, 165–166

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: http://ees.elsevier.com/gendis/default.asp

RESEARCH WATCH

Culturing human embryos beyond blastulation: Pushing the limits and exploring the unexplored

Fei Li

The Editorial Office of Genes & Diseases, Chongqing, 400046, China

Received 8 July 2016; accepted 11 July 2016
Available online 17 July 2016

KEYWORDS
Blastocyst;
Culture;
Embryonic development;
Human;
Morphogenesis

Abstract Two articles recently published in *Nature* and *Nature Cell Biology* reported that early human embryos were successfully cultured beyond blastulation. This development heralds an important step toward exploring the unknown molecular events driving human pre-gastrulation development, but it inevitably raises the ante in the decades-old ethical debate on how to define early human life and how to save human lives through research without destroying another life in the process.

Culturing early human embryos has merits in the clinical setting for *in vitro* fertilization (IVF). For this purpose, an *in vitro*-fertilized egg is cultured in suspension medium for two to six days to sustain its cleavage through the morula stage to the blastocyst stage. The selected healthy embryos are transferred into the uterus either at the pre-morula or blastocyst stage to establish pregnancy. It has been generally observed that it is difficult to keep human embryos viable in suspension culture beyond the blastocyst stage. Due to this technical barrier, the molecular events driving human embryonic development beyond the blastocyst stage are largely unexplored. Although there have been some studies based on various stages of mouse or non-human primate embryos harvested from the uterus, the findings cannot be reliably extrapolated to the human situation. To improve the survival of the embryos beyond the blastocyst stage, fallopian epithelial cells, mouse embryonic feeder cells, or ECM matrix have been used to culture attached embryos, regardless of whether they were of mouse, non-human primate, or human origin. However, these measures are mainly employed in the context of extracting pluripotent embryonic stem cells from the inner cell mass (ICM) of the blastocyst. Research aimed at early embryonic development beyond the blastocyst stage under similar extended culture protocols is a recent trend.

Using an ECM-based attachment protocol, two collaborating research teams successfully achieved the culture of

E-mail address: fei@genesndiseases.org.
Peer review under responsibility of Chongqing Medical University.

http://dx.doi.org/10.1016/j.gendis.2016.07.002

human embryos beyond the blastocyst stage.[1,2] Using this optimized culture system, the researchers compared the early embryonic structural development of the attached embryos with the historical data obtained from human embryos harvested during clinical procedures. They documented that the cultured human embryos recapitulated the early events that occur during pregnancy, such as early lineage separations and the morphogenesis of primitive embryonic and ex-embryonic tissues. The researchers analyzed and compared the gene expression patterns underlying these morphogenic events, demonstrating a previously unknown developmental autonomy of an early embryo without contact with the uterine endometrium, i.e., the real process of implantation. However, the present culture system saw a deterioration of the embryos cultured beyond day 12, suggesting that a cell—cell interaction with maternal feeder cells may be required to sustain the embryo into gastrulation, a stage when the three germ layers (ectoderm, mesoderm and endoderm) are formed. Thus, it would be interesting to compare these results with those obtained from embryos cultured with maternal feeder cells. This attempt, however, may run against the present ethical guidelines governing research on human embryos, which stipulate a 14-day culture limit. This newly reported progress heralds an important step forward in exploring the unknowns of the human development prior to gastrulation, but it inevitably raises the ante in the decades-old ethical debate on how to define early human life, as well as how to save human lives through research without destroying another life in the process.

Conflict of interest

The author declares no conflict of interest.

References

1. Shahbazi MN, Jedrusik A, Vuoristo S, et al. Self-organization of the human embryo in the absence of maternal tissues. *Nat Cell Biol*. 2016;18:700—708.
2. Deglincerti A, Croft GF, Pietila LN, et al. Self-organization of the in vitro attached human embryo. *Nature*. 2016;533:251—254.