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Reproductive System & Sexual Disorders: Current Research

Perspective

Endometrial Organoids were Generated to Simulate Physiological Responses of Reproductive Hormones

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ABOUT THE STUDY

Significant opportunities to further the study of human embryo implantation and placentation may be provided by a micro physiological model system. Technical obstacles as well as ethical concerns about studying humans could be achieved by developing such models. Micro physiological models would also make it possible to develop effective interventions in pertinent biologic systems as opposed to a "black box" model organism. Over the last ten years, advances in technology and our understanding of the biology of the endometrium have led to a variety of methods for creating an *ex vivo* model for embryo implantation. Organ-on-chip models have been developed using microfluidic culture and stem cell spheroid three-dimensional tissue system organoids to mimic key aspects of human reproduction. To name a few, there are human stem cell spheroids that resemble the blastocyst and three-dimensional platforms that model the endometrial milieu.

Benzylaminopurine treated Embryoid bodies (BAP-EB) trophoblastic spheroids were created from human embryonic stem cells. These spheroids mimicked human trophectoderm at the transcriptome level. Furthermore, the tissue produced a considerably greater implantation rate in implantation cell culture models derived from receptive endometrium. These research used rigorous and robust experimental designs and reporting. The researchers cultured BAP-EB from human embryonic stem cell lines Val 3 and H9/WA09 for 96 hours, then collected endometrial aspirates from receptive human chorionic gonadotropin-producing women.

They also compared expression in 1,529 cells (single-cell RNA sequencing) obtained from human preimplantation embryos (n = 88). (GEO Accession number GSE36552 and Array Express Accession number E-MTAB-3929), which correspond to undifferentiated or less-differentiated cells, using principal component analysis, gene expression correlation, and underlying functions ranked by gene set enrichment analysis and normalized enrichment score. Spheroids were transcriptomic ally different from developed epiblastic cells, whereas trophoectoderm was identical to them. At the level of gene expression, differentiated BAP-EB did indeed group with trophectoderm.

The authors also noted that BAP-EB differentiation is mostly mediated by hippo signalling, which is supported by the drastically decreased attachment observed when YAP1 inhibitor was used. To further support the function of E-cadherin in embryo implantation, this investigation additionally examined the molecule(s) responsible for BAP-EB attachment using an antibody blocking experiment. The procedure and setup for BAP-EB spheroid differentiation with a typical trophectoderm-like signature are the study's key contribution. This study moves us one step closer to developing an *ex vivo* model to research embryo implantation. Studies are increasingly proving the viability of such novel designs *in vitro* before translating them into practical use.

Organoid technology, a cutting-edge tool for *in vitro* minitissue growth, is one advanced of these models. Organoids has the capacity for long-term growth while maintaining molecular and functional stability. In fact, the recently developed endometrial organoids phenocopy physiological reactions to reproductive hormones and imitate the menstrual cycle in a culture plate. The organoids are derived from damaged endometrium and faithfully reproduce the abnormal tissue features of patients.

Insight into individualized medical care may also be provided by them. By using reproductive tract microfluidic culture methods, where a fluidic plate with microchannel pumps and links fluids between various tissues, it is possible to create an even more accurate micro physiological environment. By interacting with tissues and organs like the liver, ovaries, fallopian tubes, and cervix, these systems can mimic the function of the human endometrium. Based on individualized models for each patient's endometrial tissue, microfluidic technologies may offer a future tool for pharmacologic testing in female patients.

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