A Novel Patient-derived 3D Organoid of Endometriosis for Drug Evaluation

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Abstract

Endometriosis is a complicated and chronic female disorder, with clinical manifestations of dysmenorrhea, infertility, and other symptoms. Due to the obscure etiology and complex mechanism and easy recurrence of endometriosis, effective treatments are still absent in clinical practice. The existing research models include cell models, such as two-dimensional (2D) culture of cell lines or primary stromal cells derived from patients, lacking the epithelial-derived glandular structures in endometriosis tissues and losing the intercellular interactions, which may lead to distortions in mechanism research and drug evaluation. While animal models also have issues such as species differences, poor success rates in modeling, and high costs. Therefore, establishing biomimetic in vitro models using patient-derived endometriosis tissues is conducive to fundamental and applied research for drug development of endometriosis. n this study, we obtained stromal cells and epithelial organoids of glandular structures from patient-derived endometriosis tissue. The epithelial organoids could be maintained for long-term culture and passage in the Matrigel and retained good viability. H&E staining indicated that the epithelial organoids were similar to the glandular structures in the lesion tissues. IHC results demonstrated the expression of hormone receptors ER and PR, cell membrane proteins such as E-cadherin and CD44, and MMPs and their inhibitors associated with endometriosis invasion. Stromal cells expressed vimentin, maintained good cell viability, and could form 3D cell spheroids with invasion capabilities in Matrigel. To achieve the interaction between the two cell types, they were further co-cultured to simulate the tissue characteristics of endometriosis lesions. The experimental results revealed that the co-culture mixture could maintain long-term viability, offering the possibility for long-term drug evaluation. We further tested the effectiveness of the clinical drug Dienogest on the newly established model. The results showed that this drug could inhibit the proliferative activity of endometriosis epithelial organoids, stromal cells, and the co-culture mixture. The main innovation point of this study is the realization of 3D co-culture of the two key cell types in endometriosis tissues, with bionic simulation of the characteristics of endometriosis tissues, providing a new in vitro model for drug evaluation and drug development.

Keywords

Endometriosis, 3D Organoid, Drug Evaluation

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