Editorial

Miniature Biodevices with Mighty Impact: the Current Applications and Future Challenges of Organ-on-Chip Technology

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Miniature biodevices and organ-on-chips (OOC) are a revolutionary advancement in biomedical research that transforms our approach to studying human organs and tissues by providing a realistic micro-physiological system with a highly controlled environment. OOC, also known as "tissue chips," typically consists of microfluidic channels lined with living human cells that mimic the functionalities of specific organs. These cells are cultured in a controlled environment replicating the organ's microarchitecture, mechanical forces, and biochemical signaling [1]. The technology has tremendous potential to improve biomedical research techniques, but various challenges must be addressed for its broader implementation.

The ability to recreate dynamic physiological conditions, mechanical forces, and biochemical signaling in these biodevices allows researchers to investigate complex biological processes with high precision. This more profound understanding of organ physiology and disease mechanisms can lead to the development of innovative therapeutic approaches. OOC devices facilitate drug screening, allowing faster drug efficacy and toxicity assessment more efficiently than ever before. OOC models enable a more accurate representation of human physiological and pathological processes reducing the reliance on animal testing, thus offering a more ethical and cost-effective alternative. This approach can improve the success rate of drug development and lead to more personalized and targeted treatments. Personalized organ chips can reflect an individual's unique physiology by harnessing the power of patient-derived cells and mimicking the physiological and biochemical microenvironment of organs. These can provide precise information about any individual's disease mechanisms and drug responses. Researchers can tailor treatment approaches and optimize therapies based on this more profound understanding of personalized drug responses gained by creating patient-specific organ models. Organ models have been developed for almost all significant organs [2-4].

Liver-on-chip have been developed to mimic the hepatic lobules, including co-culturing hepatocytes

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with fibroblasts, using microfluidic perforations, and creating biomimetic platforms for hepatic spheroids and liver tumors. These models enable the study of drug metabolism, hepatotoxicity, and anti-cancer pharmaceutical investigations. Lung-on-chip models provide insights into respiratory processes and replicate the alveolar-capillary barrier. These models incorporate alveolar epithelial cells and pulmonary microvascular endothelial cells and simulate the expansion and contraction of alveoli during respiration. These models enable the study of lung diseases. Heart-on-chip models replicate the coupling of the cardiac and vascular systems by combining cardiomyocytes with vascular endothelial cells allowing assessment of drug effect and efficacy on the heart. Intestine-on-a-chip models mimic the composition and function of the intestine and enable drug testing, research on the gut microbiota, and investigation of intestinal illnesses. Kidney-on-a-chip models replicate renal filtration and the structural and functional attributes of the glomerular capillary membrane using renal epithelial cells and enable the study of hormone activation, molecular transport, and nephrotoxicity [2]. The technology has also been used to study the reproductive system, brain, and pancreas [5-7].

The technology also finds applications in toxicology, environmental monitoring, and disease modeling. OOC models provide a more physiologically relevant toxicity testing platform than static cell cultures or animal models [8,9]. OOC systems can potentially recreate the microenvironment of specific organs, allowing researchers to mimic disease conditions and study the underlying mechanisms, known as disease modeling [3, 10]. Using patient-derived cells, OOC models can closely replicate the characteristics of diseases such as cancer, cardiovascular disorders, and neurodegenerative conditions [3, 11]. This enables researchers to understand disease progression better, identify new therapeutic targets, and test the efficacy of potential treatments [12, 13]. Tumor-on-a-chip is one such example of disease modeling that allows the creation of chips with multiple organoids to study the penetration of cancer cells into different tissues [14, 15]. These models can potentially improve our understanding of metastasis and aid in identifying intervention targets [12, 16, 17].

OOC technologies represent a promising approach in the field of biomedical research, enabling the development of miniature, functional models of human organs [3, 18]. OOC platforms offer advantages over traditional in vitro and animal models, providing more valid and reliable systems for studying human physiological and pathological mechanisms [3,10]. However, several challenges that need to be addressed hinder the widespread practical application of OOC technology [19, 20].

One major challenge in OOC technology is accurately replicating the complex three-dimensional (3D) architecture to generate multi-OOC platforms that aim to emulate entire biological processes seldom limited to a single organ [21]. Multi-OOC technology can simulate human physiology at the level of the whole organism, offering excellent accuracy and model complexity [21]. Achieving this level of complexity requires advanced fabrication techniques and biomaterial engineering [22].

Another major challenge is long-term stability and reproducibility in the practical application of OOC technology. Preserving the viability and functionality of biological components, including cells and tissues, requires effective temperature regulation, nutrient supply, and waste removal to ensure an optimal microenvironment. Furthermore, reliable reproducibility results in long-duration studies [4, 23-25]. Another critical aspect of OOC technology is to provide the widespread acceptance and reproducibility of OOC models; there is a need for standardization and validation protocols [19, 26]. This will enable researchers to compare results among different OOC models for drug screening, toxicology studies, and disease modeling [27, 28]. In addition, there is a growing demand for developing OOC models that can simulate organ-organ interactions accurately [10, 29]. Integrating multiple organ systems within a single OOC platform presents considerable technical challenges [21, 30].

Ethical and regulatory considerations must be addressed, including issues related to the sourcing and use of human cells and establishing guidelines for preclinical drug testing using OOC models [31, 32]. Collaboration between researchers, regulatory agencies, and ethics committees is crucial to develop policies that ensure the ethical and responsible use of OOC technology [33, 34].

In conclusion, OOC technology is a revolutionary innovation in biomedical research. Combining microfluidics, tissue engineering, and cell biology provides a powerful tool for studying human organs and tissues in a physiologically relevant manner. This technology holds immense potential to transform drug

development, disease modeling, and personalized medicine, ultimately improving healthcare outcomes for individuals worldwide. However, several challenges need to be overcome for its widespread application. By addressing the complexity of tissue architecture, replicating physiological function, standardization, integrating multiple organ systems, and addressing ethical and regulatory considerations, OOC technology can pave the way for more effective and personalized approaches to disease modeling and drug development.

Consent for Publication

The author reviewed and approved the final version and has agreed to be accountable for all aspects of the work, including any accuracy or integrity issues.

Disclosure

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Data Availability

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All authors contributed significantly to the work, whether in the conception, design, utilization, collection, analysis, and interpretation of data or all these areas. They also participated in the paper's drafting, revision, or critical review, gave their final approval for the version that would be published, decided on the journal to which the article would be submitted, and made the responsible decision to be held accountable for all aspects of the work.

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