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Organ-on-chip technology's development and usages: A comprehensive review

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Abstract. Organ-on-a-chip technology is a new development technology that has made great contributions to the field of biomedicine-medicine, which began to be studied in 1950 but has not achieved effective results. With the development of technology and the passage of time, the first successful organ-on-a-chip products were introduced in 1990. Organ-on-chip technology has broken through the limitations of human drug testing and pathological research, solved the problem of unsatisfactory efficacy after using animal simulation, and greatly promoted the development of pathology and pharmacology. Organ-on-a-chip refers to the cell culture of human organs on a chip to simulate the function and characteristics of human organs, providing a new way for disease treatment and drug research and development. The researchers began by trying to grow cells on artificial substrates to mimic the structure and function of human organs. Organ-on-a-chip technology can process cell cultures while improving the environment for human drug testing and pathology research, truly "simulating and performing experiments on humans." Organ-on-a-chip is a cell culture analog that utilizes a microfluidic device in which microchannels are used to guide and manipulate the solution. In recent years, with the development of bio print technology, the research of organ chips has entered a new stage. Bioprinting allows cells and biomaterials to be arranged in predetermined patterns and structures to build tissues and organs with specific functions. At present, the research of organ chips can already help us complete the test drug and case analysis, the development time of this technology is very short, and there is still a lot of development and exploration space in the future.

Keywords: Organ-on-chip Technology, Biomechanics, Clinical Medicine, Biology, Mechanics.

1. Introduction

Organ-on-a-chip technology is an invention that combines biology with microtechnology to simulate key aspects of human physiology. As an effective simulator of human disease, it offers unique opportunities for medical and physiological research at the micro-scale. Before the advent of organ-on-a-chip technology, most scientific drug experiments on humans were based on animals, such as rabbits, mice, and monkeys. It is undeniable that animal models do make great contributions to the field of medical science, but there are differences between people and animals that cannot be ignored, many drugs in animals cannot reflect the full effect, and there are many genetic and physiological structure differences between animals and humans, many drugs in animals will appear in humans will not reflect toxicity [1].

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According to statistics, more than 80% of drugs based on animal models fail clinically, 60% are ineffective, and 30% are toxic because they do not appear in animals. In this case, a drug experiment instrument that can completely simulate the human body has become a modern scientific research technology. So scientists have come up with a concept: cell culture analogy. It is "specifically designed to grow mammalian cells in interconnected chambers perfused with circulating tissue medium or 'blood substitute.'" Under this concept, the first embodiment of organ-on-a-chip technology: the heart and lung microcomputer was developed. Cardiopulmonary microcomputers are the product of combining lung cell culture models with cardiac devices to evaluate the effects of drugs and treatments injected into the human lungs via aerosols on cardiac function and toxicity in vitro. The invention and trial also laid the foundation for future organ-on-a-chip technology [2].

Today's organ-on-a-chip technology takes the form of microfluidic devices, which contain a network of hair-thin microchannels to guide and manipulate tiny volumes of solution. The organ here does not mean an actual organ, but a tiny tissue that grows on a microfluidic chip. Organ-on-a-chip can be thought of as a bridging technology that provides the ability to process cell cultures while also providing a better-engineered microenvironment to maximize the trustworthiness of the model.

Organ-on-a-chip technology has become a breakthrough for studying human organs and tissues in a controlled, micro-engineered environment. Due to the need to better understand the human physiology behind health and disease, and to find new ways that can improve the human condition, OOC technology is advancing day by day. This technology has the potential to revolutionize drug development, disease modeling, and personalized medicine. In this article, we will explore the development of organ-on-a-chip technology and its various applications, with a primary focus on understanding the key advances, challenges, and prospects of this innovative technology to help understand where the technology is now and where it can be further studied [3-4].

2. Development of Organ-on-Chip Technology

The development of organ-on-chip technology has been driven by the need for more predictive and reliable models for drug testing and disease research. Early pioneers recognized the limitations of traditional in vitro and animal models, which often fail to mimic the complex physiological interactions occurring within human organs. The integration of microfabrication techniques, microfluidics, and cell biology has allowed researchers to create microscale devices that emulate the structural and functional aspects of specific organs.

The initial examples of organ-on-chip focused on specific organs such as the liver, lung, heart, and intestine. These devices consist of microfluidic channels lined with human cells, capable of replicating the organ's native microenvironment. By recreating the physiological conditions, researchers can observe how cells interact, respond to stimuli, and enable drug absorption, metabolism, and toxicity testing [5-6].

3. Applications of Organ-on-Chip Technology

3.1. Disease Modeling

Organ-on-chip technology offers a novel platform for modeling diseases in a physiologically relevant manner. Researchers can use patient-derived cells to recreate disease-specific microenvironments and evaluate disease progression, drug response, and potential therapeutic interventions. This approach has been particularly useful for studying complex diseases such as cancer, neurodegenerative disorders, and genetic disorders. In the article "Human Organoids and Organs-on-Chips for Addressing COVID-19 Challenges", the researcher demonstrated that the organs-on-chip technology helped people to try vaccines and treatments, it also helped humans to simulate the infection environment [7].

3.2. Drug Screening and Development

Traditional drug development processes rely heavily on animal models, which often fail to accurately predict human responses. Organ-on-chip platforms provide a more human-centric approach to drug

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screening and development. They allow for high-throughput testing of drug efficacy, side effects, and toxicity, reducing reliance on animal testing and increasing the efficiency of drug discovery. The article "A new paradigm for drug development" mentioned: That organ-on-a-chip, a cutting-edge technology that can emulate the physiological environment and functionality of human organs on a chip for disease modeling and drug testing, shows great potential for revolutionizing the drug development pipeline. The article "Organ-on-a-chip, an introduction to its functions and applications" mentioned that drug testing in the pharma industry is crucial to ensure proper function, and OoC can help with these kinds of problems [8].

3.3. Medicine

For all medicines' development, in drug therapy, inappropriate use of drugs, such as mismedication or overdose, often occurs in cases of drug-induced kidney injury, damaging human health and bringing unintended consequences. Understanding the mechanisms by which drugs trigger nephrotoxicity can help in the development of safer drugs and can also help determine the appropriate dosage for the safe use of drugs. Because in vitro models of the kidney are difficult to effectively simulate in vivo conditions, there is still no suitable in vitro model that can be used to predict the damage caused by drugs to the kidney. The development of organ-on-a-chip technology has opened up new ways to evaluate drug nephrotoxicity so that the problem is no longer "unsolvable". In addition, the organ that plays a key role in drug metabolism is the liver, and organ-on-a-chip technology can help understand the drug efficacy and potential liver toxicity during drug use, contributing to safer drug use. The unique high-throughput screening technology of organ-on-a-chip has the advantages of genetic stability and scalability. Studies have been conducted using lung and colon organoids constructed from human pluripotent stem cells for high-throughput screening. From a variety of drugs approved by the US Food and Drug Administration, it has been identified that drugs including imatinib, mycophenolic acid, and quinacrine dihydrochloride can prevent SARS-CoV-2 from entering lung organoids and inhibit viral infection in colon organoids. The above organoid models are validated for screening drug candidates in patients with COVID-19. The main research content of organoid-related clinical trials is to explore and establish various organoid models of human samples for the evaluation and prediction of drug sensitivity, efficacy, and prognosis, and the study of disease mechanisms, to explore the feasibility of using them to guide the selection of individual treatment programs. For example, the clinical trial "The role of tumor-immune microenvironment organoids in predicting immune-related adverse events", registered in May 2023, mainly uses organoid technology to study biomarkers of adverse events related to lung cancer to further confirm treatment options and drug options.

This technology also contributed to medicine personalization. Organ-on-chip technology has the potential to revolutionize personalized medicine by enabling the testing of individual patient responses to drugs and therapies. By using patient-derived cells, researchers can create personalized organ-on-chip models to mimic the patient's specific physiology and evaluate treatment outcomes. This approach promises to optimize treatment strategies, reduce adverse effects, and improve patient outcomes.

4. Advancements and Challenges

Since the development of new drugs requires a large amount of money in vitro and animal tests in the preclinical stage, and there is a greater risk of failure in the late stage, it will cause a certain degree of waste of resources.

However, organ chips can not only make up for the shortcomings of 2D culture in vitro which cannot reflect the complex role of the human body or extracellular environment, but also make up for the resulting error caused by the biological differences between animal models and humans.

Organ chips can reproduce key dynamic processes, linking with biosensors to allow real-time online measurement of cell viability and function. This technology can also culture cells in a certain direction and a unified way, overcoming the challenges of producing organoids of uneven size and

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controlling cell proportion in the self-organization process of organoid culture, making the product more reproducible.

However, there are some challenges with the chip model. Suitable cell-fluid ratios and surface-volume ratios in the chip model still need to be explored, and unsuitable ratios can affect cells and observations. In addition, there is no standardized specification for organ chips, making it difficult for researchers to conduct research according to established standards, which will increase the probability of experimental error.

Significant advancements have been made in organ-on-chip technology, including the integration of multiple organ systems, the incorporation of immune cells, and the development of dynamic and biomimetic microenvironments. These advancements have increased the sophistication and relevance of organ-on-chip models, bringing them closer to replicating the complexity of human organs.

However, several challenges still need to be addressed. Standardization of protocols, reproducibility of results, and scalability of organ-on-chip platforms are critical aspects that need further development. In the essay "An investigation of OOC test results and problems", the author mentioned that a difficult goal that needs to be achieved is the body-on-a-chip concept, which requires multiple OOCs of different cell types or organs to be linked to create a system [9]. Additionally, there is a need to improve the complexity and interconnectivity of organ-on-chip systems to simulate the interactions between different organs accurately.

The prospects of organ-on-chip technology are promising. With ongoing advancements in microfabrication, biomaterials, and bioengineering techniques, organ-on-chip models will become increasingly physiologically relevant and predictive. The integration of artificial intelligence and machine learning algorithms will further enhance the interpretation and analysis of organ-on-chip data.

5. Conclusion

Organ-on-chip technology has emerged as a powerful tool for studying human organs and tissues in vitro. Its development has shown significant progress in recreating complex organ microenvironments and providing physiologically relevant models for drug development and disease research. Despite existing challenges, combining multidisciplinary research, technological advancements, and continued collaborations will drive the field forward. Organ-on-chip technology is poised to revolutionize the biomedical field, ultimately leading to improved therapies, personalized medicine, and a better understanding of human physiology and diseases.

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