A review of the research progress of organ chips in the field of biomedicine

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Abstract: Organ chips is a cutting-edge frontier science in the field of life sciences. It has broad application prospects and development space in the fields of tissue and organ development, disease mechanism research, new drug evaluation and selection, and biological research, and it has significant strategic significance for supporting the development of innovative drugs and translational medicine. This review summarizes the current research status, challenges, and application prospects of organ chips technology in the field of biomedicine both at home and abroad.

Keywords: Organ Chip; Biopharmaceuticals; New Drug Development; Drug Evaluation

Currently, animal experiments remain the principal research approach for evaluating the preclinical safety and efficacy of drugs during the process of new drug development. Nevertheless, a growing body of evidence indicates that animal models lack sensitivity and specificity in predicting human drug toxicity [1], and they encounter problems such as lengthy durations and ethical considerations in experiments. Simultaneously, with the escalating demand for various novel drug developments such as gene-modified cell therapy and multi-functional antibodies, new drug research and development confronts scenarios of heightened difficulty in achieving success, rapid expansion of the types of drugs under development, and escalating research costs. Against this backdrop, the development of organ chip technology with higher biomimetic degrees is attracting increasing attention in the biomedical domain.

1. The development course of organ chip technology

1.1 Conceptual definition

The organ chip takes microfluidic control chip technology as the core and integrates multiple approaches such as cell biology, biomaterials, and engineering to simulate and construct an in vitro tissue and organ microenvironment that encompasses complex factors such as various living cells, functional tissue interfaces, biological fluids, and mechanical force stimuli. It constitutes a physiological microsystem built on a chip [2], reflecting the functional characteristics of the major structures and organs of the human body. It can be generally understood as: through the construction of a simplified version of human tissues and organs on a chip, the core biological functions of human tissues and organs are simulated and reflected in vitro, and this is achieved by preserving the fundamental biological structures.

1.2 Development history

The origin of organ chip technology can be traced back to the 1990s when the National Institutes of Health in the United States attempted to fabricate miniature organ models using microfabrication techniques. In 2010, scholars such as Donald Ingber from Harvard University first published the research results of lung organ chips in the journal Science. They constructed an upper and lower layer space inside the chip, where the upper layer space was for gas flow, and the bottom layer space was for blood flow with human lung epithelial cells and vascular endothelial cells isolated in the middle. The entire cavity formed a structure and function similar to alveoli through the construction of the upper and lower layer spaces inside the chip, and could simulate the basic physiological characteristics of the lungs in drug treatment and lung disease experiments. Through the stretching of the flexible structures on both sides, the effects of expansion and contraction were achieved. In recent years, with the rapid development in the fields of tissue engineering and precision processing technology, based on traditional organ chips, organoids-on-chips are a typical cross-cutting frontier science and technology, and have emerged as a new research direction in the biotechnological field that integrates multiple disciplines such as physics, chemistry, biology, medicine, materials science, engineering, and micro-electromechanical systems. It is also a relatively typical new high-quality productive field in the future.

2. Organ-on-a-chip Advantages, Limitations, and Types of Functions

2.1 Advantages, Limitations, and Types of Functions

Organ-on-a-chip technology has the following advantages: First, high biomimicry degree. It can simulate more realistic and reliable human organ structures and functions, providing a more realistic environment for drug screening and evaluation. Second, high efficiency. It can conduct multiple drug screening and evaluation simultaneously, thereby improving the efficiency of drug development. Third, repeatability. The reproducibility of experimental results has a positive promotion effect on improving the success rate of drug development, reducing risks, and lowering research costs. Fourth, effectively solving the ethical issues involved in medical research using animals. Based on these characteristics, the application areas of organ-on-a-chip technology are very broad, and it has made good progress in drug development, drug toxicity assessment, and disease model research in the field of biomedicine. At the same time, the development of organ-on-a-chip still faces many challenges, such as the most core technical link, the overall level of organization and organ simulation in existing models is still relatively preliminary, especially the establishment of neural, vascular, immune systems and microenvironment in organoids still has a large number of bottleneck problems to be overcome [3]. In addition, the problem of cell source, how to achieve high-throughput screening and online detection, the optimization of chip materials, the standardization of organ-on-a-chip, and the integrated development of multi-organ-on-a-chip, still need further exploration and improvement.

2.2 Current Typical Types of Organ-on-a-chip

Brain. Generally, a dual channel structure with a middle porous polycarbonate membrane septum controlled by two sets of flow path systems is used to simulate the formation of a blood-brain barrier structure in the body by the neurovascular units at the ends of blood vessels and nerves. One channel of the chip is composed of astrocytes, and the other channel is composed of brain microvascular endothelial cells, which are cultured by constant flow rate perfusion.

Liver. Establishing liver physiological models for drug development and toxicology research on chips, such as bile duct, hepatic lobule, and hepatic sinusoids models. The advantage of the chip liver model is that it can form micrometer sized cell clusters over a long period of time, with partial liver function, thereby forming a liver model that maintains liver specific function similar to human morphology.

Kidneys. Constructing an integrated microsystem using microfluidic control chip system, with the main goal of simulating in vitro renal function, to enhance the control capabilities of microfluidics, cells, and their microenvironments. The emergence of renal chip technology provides a research model that is closer to the real physiological and pathological conditions of the human body for evaluating the effectiveness and safety of drugs and vaccines, while also offering lower costs for biomedical research.

Lungs. Contains upper and lower channels, separating the two channels into a soft porous membrane. Cultivate different cells on both sides of the membrane: the upper channel is human alveolar epithelial cells, and the lower channel is human pulmonary microvascular endothelial cells. Cultivate different cells on both sides of the membrane: the upper channel is human alveolar epithelial cells, and induce the cultivation of endothelial and epithelial cells in the micro device of the lung chip, which can display complex physiological functions at the organ level.

Heart. It can simulate different characteristics of the heart, such as mechanical contraction, molecular transport, electrical stimulation, and specific responses to certain drug stimuli. Cultivate different types of cells to produce suitable cardiac tissue, such as cardiomyocytes, endothelial cells, etc., and generate corresponding cardiac tissue in microfluidic channels. In addition, the complex myocardial tissue architecture has been accurately studied in cardiac chip organ models, simulating the shear stress caused by blood flow on myocardial tissue through continuous perfusion of culture media.

Construction of a multi type organ chip system. The connection between multiple organs has gradually become a new direction for research in this field. There are natural connections between human tissues and organs, and most physiological functions or diseases occur under the joint action of multiple organs. At present, researchers have conducted preliminary explorations in this direction and established a series of organoid co culture systems. If iPSCs are used to achieve simultaneous cultivation of three interconnected organoids, namely the liver, bile duct, and pancreas; The cultivation of brain organs and the establishment of connections between the brain and visual cup structures in the development of simulation eyes.

3. Current situation of industrialization development

From the perspective of market size, according to Allied Market Research analysis, the value of the organ chip market was $103 million in 2020, and it is expected to reach $1.6 billion by 2030, with a compound annual growth rate of about 31%.

From the perspective of business models, the main business models of the global organ and organ chip industry include direct sales of products and provision of services. According to the White Paper on Organoids and Organ Chips, which surveyed 49 related companies worldwide, the development path of this industry will include the fields of precision instruments and equipment, CRO services, and biotechnology. 80% of enterprises in this field provide services such as organoid chips and imaging devices, while their product areas are concentrated in the upstream of the industry chain, providing automated high-throughput operators, chip manufacturing and other instruments and equipment.

From the perspective of application fields, it includes disease modeling, toxicity testing, high-throughput drug screening, drug evaluation, extended drug indications, precision cancer treatment, regenerative medicine, and space medicine. The currently mature application scenarios are in fields such as drug evaluation and drug safety testing.

From the perspective of enterprise layout, the global market concentration of the organ chip industry is relatively high, with North American and European manufacturers as the main players. Representative companies include eMulate, Mimetas, Tissus, ValHealth, etc. Among them, the top 3 companies have a market share of 44.87%, with eMulate having the highest market share of around 15%.

China's basic research on organ chips has made significant breakthroughs in the past few years, forming multiple research units and universities with distinctive development characteristics, including the Chinese Academy of Sciences, Zhejiang University, Shanghai Jiao Tong University, Tsinghua University, and Peking University. However, the commercialization of Chinese organ chips is still in its infancy. In 2022, the market size of Chinese human organ chips will be about US $0.05 billion, accounting for 5.69% of the global market share.

4. Summary and Prospect

As a cutting-edge technology in preclinical research, organ chips have more functions, higher integration, higher automation, and stronger personalization, gradually changing the way medical research is conducted. There is great potential in fields such as disease research, toxicity prediction, personalized medicine, and new drug development. With the maturity of technology, future complete life simulation systems are expected to be constructed through the combination of multiple organ chips, which will provide more comprehensive and efficient solutions for research in many disciplines including life sciences and medicine.

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