Organ-on-a-Chip technology: the key to reducing animal testing

Authors: Eline Geervliet, Suzie Grigorjan, Susan Roelofs

Limitations of animal testing

Animal testing has played a vital role in advancing medical research by contributing to breakthroughs in drug development, drug safety, and disease understanding. However, despite these contributions, animal testing comes with significant limitations. Ethically, the practice raises serious concerns about animal welfare, prompting growing public opposition and calls for more humane alternatives [1]. Scientifically, animal models often fall short in accurately predicting human responses due to species differences in genetics, physiology, and metabolism, which can lead to unreliable results and failures in later-stage human trials [2]. Moreover, animal testing is highly costly, demanding substantial financial and infrastructural resources [2].

These combined ethical, scientific, and financial challenges highlight the pressing need for innovative, human-relevant testing methods, with organ-on-chip technologies serving as a promising complementary approach that can help advance the 3R (Replace, Reduce, Refine) strategy in both the EU and the USA

Organ-on-a-chip as alternative

Organ-on-a-Chip (OoC) technology leverages advanced microengineering techniques to mimic the functions of human organs within a microfluidic device. These chips typically consist of transparent polymers like PDMS, embedded with a network of microchannels lined with living human cells. The channels are designed to replicate key physical and biochemical cues present in human tissues,such as fluid shear stress, mechanical strain, and chemical gradients.

An example is the, lung-on-a-chip model, which includes a flexible membrane that could simulate the stretching of lung tissue during breathing. By precisely controlling the microenvironment, these platforms enable researchers to observe cellular behavior and organ-level responses in real-time. Unlike animal models, OoC systems offer species-specific human data, eliminating discrepancies caused by cross-species differences and providing a more physiologically relevant alternative for studying disease progression, drug efficacy, and toxicity [3].

The role of barrier integrity analysis in reducing animal models

Crucial in the endeavor of reducing animal models is ensuring the quality and physiological relevance of in vitro systems, and organ-on-a-chip technologies. Many organ systems, such as the gut, lung, and blood-brain barrier, rely on tightly regulated cellular barriers to maintain homeostasis and control permeability.

Measuring the integrity of these barriers, with e.g. a transepithelial electrical resistance (TEER) measurement, provides critical validation that the chip accurately replicates native tissue functions [4]. This is particularly valuable in drug testing, toxicity screening, and disease modeling, where barrier dysfunction is often a key factor.

For example, blood-brain barrier-on-a-chip models are used to evaluate the ability of therapeutic compounds to penetrate the central nervous system, while gut-on-a-chip devices allow researchers to study drug absorption and inflammatory diseases. By providing robust, human-relevant data, barrier integrity analysis strengthens the case for organ-on-a-chip technologies as viable alternatives to animal testing.

Challenges & future directions

Despite the innovative potential of OoC technologies, several challenges remain. One of the biggest challenges lies in the complexity of replicating the interactions within human organs, particularly when integrating multiple organ systems on a single platform. Standardization is another critical issue, with a lack of universally accepted protocols and materials hindering reproducibility and large-scale production. Additionally, replicating physiologically relevant conditions, such as organ sizes, transport rates, and inter-organ interactions, requires careful balancing of numerous parameters [5].

Nevertheless, the field is progressing rapidly, paving the way for dedicated body-on-a-chip platforms and personalized medicine with patient-derived cells [5]. Furthermore, integrating these platforms with artificial intelligence and machine learning could enhance data interpretation and predictive capabilities, accelerating the shift away from animal models entirely.

Conclusion

In summary, while animal testing has historically contributed to medical advancements, its ethical, scientific, and financial limitations underscore the urgent need for more accurate and humane alternatives. OoC technology presents a transformative solution, offering human-relevant data through precisely engineered microenvironments that closely mimic organ functions. The incorporation of barrier integrity analysis further enhances the reliability and quality control of these models, ensuring their physiological relevance across various applications, from drug testing to disease modeling. Though challenges like standardization and multi-organ integration persist, ongoing advancements and collaborations within the scientific community signal a promising future. While the systems and technologies evolve toward more personalized and complex models, OoCs are the key to significantly reduce, and potentially replace, the need for animal testing altogether.

Join the conversation

Are you working with OoCs platforms? Are you working with a single organ or multiple organs on your chip?

References

[1] A. K. Kiani *et al.*, "Ethical considerations regarding animal experimentation," *J Prev Med Hyg*, vol. 63, no. 2 Suppl 3, p. E255, Jun. 2022, doi: 10.15167/2421-4248/JPMH2022.63.2S3.2768.

[2] G. A. Van Norman, "Limitations of Animal Studies for Predicting Toxicity in Clinical Trials: Is it Time to Rethink Our Current Approach?," *JACC Basic Transl Sci*, vol. 4, no. 7, p. 845, Nov. 2019, doi: 10.1016/J.JACBTS.2019.10.008.

[3] C. M. Leung *et al.*, “A guide to the organ-on-a-chip,” *Nature Reviews Methods Primers 2022 2:1*, vol. 2, no. 1, pp. 1–29, May 2022, doi: 10.1038/s43586-022-00118-6.

[4] B. Srinivasan, A. R. Kolli, M. B. Esch, H. E. Abaci, M. L. Shuler, and J. J. Hickman, “TEER measurement techniques for in vitro barrier model systems,” *J Lab Autom*, vol. 20, no. 2, p. 107, Apr. 2015, doi: 10.1177/2211068214561025.

[5] S. K. Srivastava, G. W. Foo, N. Aggarwal, and M. W. Chang, “Organ-on-chip technology: Opportunities and challenges,” *Biotechnology Notes*, vol. 5, pp. 8–12, Jan. 2024, doi: 10.1016/J.BIOTNO.2024.01.001.