Comparing Transwell and Organ-on-Chip Cultures in Modern Biology

Authors: Eline Geervliet, Suzie Grigorjan, Susan Roelofs

What is an Organ-on-a-Chip?

An Organ-on-a-Chip (OoC) is a groundbreaking bioengineering technology that mimics the structure and function of human organs on a small, microfluidic device. These chips are designed to replicate key physiological processes, using living cells and microchannels to simulate blood flow, tissue interactions, and organ-specific behaviours. OoCs are revolutionizing the landscape of drug testing, disease modelling, and personalized medicine by providing a more accurate and ethical alternative to traditional animal testing [1].

Before OoC technology revolutionized in vitro research, Transwell culturing was a novel and more representable in vitro culturing method compared to conventional 2D flat surface culturing. This traditional method involves a porous membrane that separates two compartments within a culture well, allowing cells to grow on either side while enabling controlled exchange of nutrients, gases, and signaling molecules. By mimicking tissue barriers like the gut lining, blood-brain barrier, or lung epithelium, Transwell systems provided researchers with valuable insights into cell communication, permeability, and drug transport.[2].

What are the advantages of OoCs compared to Transwell cultures?

While Transwell culturing was a significant step forward in modelling human physiology, it has limitations that OoC platforms overcome. OoCs are more physiologically relevant compared to Transwell cultures because of:

- Implementation of mechanical stimuli: Mechanical stimuli such as (shear) flow, compression and stretch improve in vivo-like cell differentiation and tissue development [3].
- Implementation of multiple cell types or tissues: OoCs enable incorporation of multiple cell types in an organ specific chip, but also enable incorporation of multiple organs on a single chip. This complexity assures in vivo-like cell-cell interaction and tissue-tissue interaction [4].
- Controlling of cell microenvironment: Interaction with non-cell substances such as the ECM and soluble factors greatly influences the cellular behaviour. This microenvironment is controllable in an OoC and therefore more representative compared to a Transwell system [1].

What are the advantages of Transwell cultures compared to OoCs?

The advantage that the OoCs are physiologically more relevant than the Transwell solution directly leads to the disadvantage that the system is more complex which leads to [1]:

- Higher costs: OoCs require specialized equipment, microfabrication techniques, and expertise, making them more expensive and technically demanding to set up compared to simple Transwell systems.

- Limited standardization: OoCs can be completely adjusted to a specific niche in biomedical research and pharmacology. While this is highly desired in the search for disease understanding and treatment, it greatly reduces the standardization and reproducibility.
- Lower throughput: OoC's are more difficult to scale-up as chips are mostly custom designed and larger compared to a single Transwell.

Conclusions

In conclusion, organ-on-a-chip (OoC) technology represents a major leap forward in in vitro modelling, surpassing traditional Transwell cultures by offering greater physiological relevance through mechanical stimuli, multi-cell type integration, and precise microenvironment control. While these advantages make OoCs powerful tools for drug development and disease research, challenges such as high costs, limited standardization, and lower throughput remain hurdles to widespread adoption. Despite these limitations, the continued development of OoC platforms holds immense promise for transforming biomedical research, while reducing reliance on animal testing. As technology progresses, further refinements may overcome these challenges, making OoCs even more accessible and impactful in the future.

Join the conversation

Are you currently working with OoCs, why or why not?

References

[1] 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.

[2] A. Kurmashev *et al.*, "Transwell-Based Microfluidic Platform for High-Resolution Imaging of Airway Tissues," *Adv Mater Technol*, vol. 9, no. 20, p. 2400326, Oct. 2024, doi: 10.1002/ADMT.202400326.

[3] K. Kaarj and J. Y. Yoon, "Methods of Delivering Mechanical Stimuli to Organ-on-a-Chip," *Micromachines 2019, Vol. 10, Page 700*, vol. 10, no. 10, p. 700, Oct. 2019, doi: 10.3390/MI10100700.

[4] Q. Ramadan, R. Hazaymeh, and M. Zourob, "Immunity-on-a-Chip: Integration of Immune Components into the Scheme of Organ-on-a-Chip Systems," *Adv Biol*, vol. 7, no. 12, Dec. 2023, doi: 10.1002/ADBI.202200312.