

Miniature organs grown in the lab can accelerate personalized medicine

Organoids, simplified miniature organs that reflect the function and structure of their parent tissues, are a recent development in biomedical research. Organoids can be grown from patient tissue, including tumours, thus offering valuable insights into the disease process and potential therapeutic targets. This technology will likely have a key role in advancing the implementation of personalized medicine.

Organoids are emerging as promising model systems for both research and clinical applications

Organoid systems were developed in response to the need for a model that can accurately represent the microenvironment and complex interactions within organs or tumours. Traditionally, mouse models and cell culture have been the main model systems for biomedical research, but they have limitations. Cell culture cannot reproduce the microenvironment and tissue architecture. Mouse models are time-consuming and applying the findings to humans can be challenging due to differences in physiology. The emergence of organoid models has enabled researchers to answer questions that could not be solved with previously existing methods.

To create organoids, stem cells are extracted and stimulated to proliferate and differentiate into the constituent cell populations of the tissue. The cells organize themselves into a structure that resembles the parent tissue^{1,2}. Organoid model systems are evolving rapidly and have the capacity to represent increasingly complicated systems. Remarkably, studies reported the development of neuronal organoids that form functional circuits resembling cortico-motor and cortico-striatal pathways^{3,4}. These advances pave the way for scientific breakthroughs in physiology to better understand how organ systems develop and interact with one another.

In addition to their value as a scientific model, organoids have great potential in personalized medicine. An important advantage is that organoids can be created from patient samples thereby producing a model that reflects the patient's unique genetics². Currently, clinicians can predict a tumour's drug sensitivity and resistance based on information from an oncology workup, but organoids will enable clinicians to validate these predictions on a representative model system before treating the patient. Another advantage is that organoids can be produced in large numbers in a relatively short time frame compared to alternative methods like tumour xenografts in mice. Rather than waiting months, the drug screening results can be ready in a few weeks. Thus, in the future, organoids may become a key step in personalized medicine workflows.

Perspectives on the future of organoid technology and its impact on medicine

To date, organoid systems have been adopted by many academic centers worldwide, including McGill, for research. However, organoids are not yet ready for clinical applications. Each organoid system would need to undergo rigorous validation to ensure that they accurately represent the disease process and responses to therapy. Validation is in progress for certain organs and tumours such as glioblastoma², but could take years for each organoid model.



MSS Tech in Health News and Views Article 2, February 2022

Moreover, personalized medicine applications require large scale production of organoids and to this end, researchers are developing automated and high-throughput systems to grow, manipulate, and analyze the organoids⁵. Considering these factors, it will likely take at least a decade or two before organoids are implemented into personalized medicine workflows. Although the wait is long, the potential benefits and implications for personalized medicine are significant.

This new technology could offer important diagnostic and prognostic information and may have a major role in determining what medications are best suited for the patient. Pathologists and oncologists would likely have the most exposure to the clinical applications of organoids, but all clinicians will probably be exposed to organoids, considering their potential for tailoring treatment to each individual. Future clinicians might also expect to increasingly see the application of organoids to the development of novel therapies in the literature. Organoids make excellent pre-clinical models to test the therapeutic efficacy before moving onto clinical trials. Looking at the bigger picture, the development of organoid technology is part of a broader trend of advancing biomedical technologies which is making personalized medicine more feasible.

Organoids are a new model system that has the potential to represent the structural and functional complexity of tumours and organ systems. This technology could lead to other scientific advancements and accelerate the implementation of personalized medicine. Although it is not yet ready to be deployed in clinical settings, it is a technology worth watching out for. By the time the current cohort of medical students finishes training and begins their careers, organoids may have been introduced to clinic and could change the way personalized medicine is practiced.

Written by: Michael Luo and the TiH Publications Team

References

- 1 Kim, E. *et al.* Creation of bladder assembloids mimicking tissue regeneration and cancer. *Nature* **588**, 664-669, doi:10.1038/s41586-020-3034-x (2020).
- 2 Jacob, F. *et al.* A Patient-Derived Glioblastoma Organoid Model and Biobank Recapitulates Inter- and Intra-tumoral Heterogeneity. *Cell* **180**, 188-204.e122, doi:10.1016/j.cell.2019.11.036 (2020).
- 3 Andersen, J. *et al.* Generation of Functional Human 3D Cortico-Motor Assembloids. *Cell* **183**, 1913-1929.e1926, doi:10.1016/j.cell.2020.11.017 (2020).
- 4 Miura, Y. *et al.* Generation of human striatal organoids and cortico-striatal assembloids from human pluripotent stem cells. *Nat Biotechnol* **38**, 1421-1430, doi:10.1038/s41587-020-00763-w (2020).
- 5 Renner, H. *et al.* A fully automated high-throughput workflow for 3D-based chemical screening in human midbrain organoids. *eLife* **9**, doi:10.7554/eLife.52904 (2020).