

COMMENTARY

Organoids: Current status and prospects (2025)

Wei Chen¹, Leping Yan^{1*}, Joaquim M. Oliveria^{2,3}, Rui L. Reis^{2,3}, Changhua Zhang¹, and Yulong He^{1*}

¹Guangdong Provincial Key Laboratory of Digestive Cancer Research, Digestive Diseases Center, The Seventh Affiliated Hospital of Sun Yat-sen University, Shenzhen, Guangdong, China

²3B's Research Group, I3Bs—Research Institute on Biomaterials, Biodegradables and Biomimetics, University of Minho, The European Institute of Excellence on Tissue Engineering and Regenerative Medicine, Guimarães, Portugal

³ICVS/3B's—PT Government Associate Laboratory, University of Minho, Barco, Guimarães, Portugal

*Corresponding authors: Leping Yan (yanlp3@mail.sysu.edu.cn); Yulong He (heyulong@mail.sysu.edu.cn)

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Abstract

Organoids have attracted increasing attention from academia, industry, and regulatory agencies. At the turn of 2025–2026, we review recent breakthroughs in organoid technology and outline the major challenges currently faced in the field. We encourage broader participation to advance organoid technologies, overcome key bottlenecks, and further enable applications in disease research and innovative drug development.

Keywords: Organoid; Progress; Bottlenecks; Drug development

The development of organoid technology is closely linked to advances over decades of epithelial stem cell research. Key milestones—including the identification of epithelial stem cells, the elucidation of molecular mechanisms governing the maintenance of stemness and differentiation, the discovery of microenvironmental factors regulating stemness and proliferation, and the adoption of three-dimensional culture systems based on basement membrane-derived hydrogels—collectively paved the way for the emergence of classic organoid technology (Figure 1). The team led by Hans Clevers at the Hubrecht Institute in the Netherlands played a pivotal role in establishing and advancing modern organoid culture methods.¹

Since its introduction in 2009, classic organoid technology has experienced rapid development. The technology is maturing gradually, and its applications have expanded considerably. With the increasing number

of commercial reagent suppliers entering the market, the cost of organoid culture has steadily decreased, facilitating broader adoption of organoids in research settings. In addition to supplying culture media, numerous companies now focus on developing organoid-specific culture equipment, *in vitro* diagnostic devices for clinical organoid drug testing, pre-clinical drug evaluation services for pharmaceutical companies, and solutions for organ regeneration, further accelerating the advancement of organoid research and application.

As an *in vitro* model for biomedical research, organoids can be expanded long-term in culture from both normal and malignant human tissues. In studies of cell physiology, non-malignant disease, and cancer, they often provide greater physiological relevance than traditional two-dimensional cell culture. Furthermore, pluripotent stem cell-derived organoids enable *in vitro* studies of traditionally

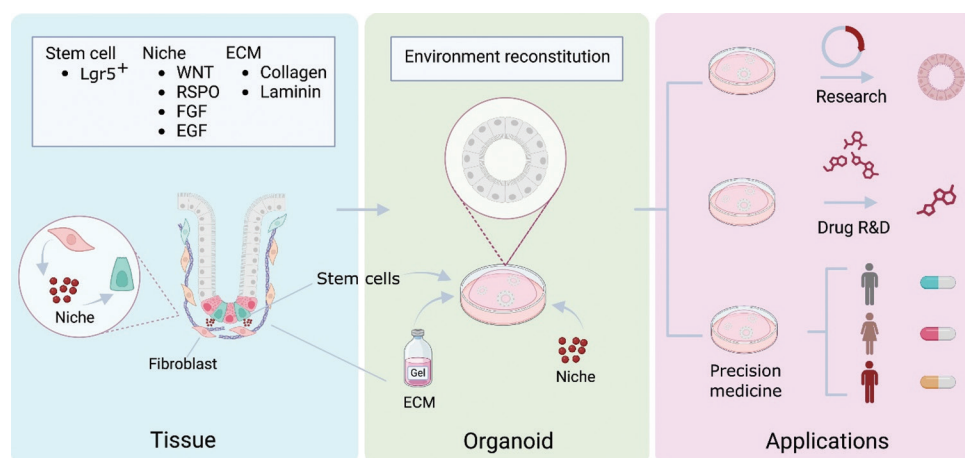


Figure 1. The principles of organoid culture and its potential applications. Organoid culture relies on reconstituting the microenvironment of epithelial stem cells *in vitro*. This microenvironment comprises stem cells, their niche, and the ECM. Using intestinal organoids as an example, Lgr5⁺ cells represent the stem cell population; niche factors, such as Wnt agonists and growth factors, are primarily produced by fibroblasts; and the ECM is composed of basement membrane components, including collagen and laminin. Organoid models offer diverse applications, primarily in basic research, drug discovery and development, and precision oncology. Created with BioRender.com.

Abbreviations: ECM: Extracellular matrix; EGF: Epidermal growth factor; FGF: Fibroblast growth factor; R&D: Research and development; RSPO: R-spondin protein.

“non-culturable” tissues, such as neuronal and cardiac tissues.² The development of organ-on-a-chip platforms by combining organoids with microfluidics enables complex cell co-cultures. Organ-on-a-chip platforms are also capable of modeling complex cell interactions, simulating tumor microenvironments, and facilitating multi-modal real-time observation, thereby enhancing their utility as research models.³ Since organoids can recapitulate the heterogeneity of patient-derived tumors and their microenvironments, they offer a more accurate simulation of complex and variable human tumors compared to models such as cell line-derived xenografts, patient-derived xenografts, genetically modified tumor models, and carcinogen-induced tumor models.

Given the role of organoids in drug efficacy and toxicity studies, pharmaceutical companies are gradually incorporating organoid testing into their pre-clinical drug evaluation procedures.⁴ Tumors exhibit significant heterogeneity, and drugs often demonstrate efficacy only in specific subtypes. The ease of establishing a large library of organoids facilitates the identification of sensitive tumor subtypes responsive to a target drug. Drug safety evaluations based on organoid models also yield promising results, aiding in the detection of potential toxic effects that may be difficult to observe in animal models, thereby reducing the risk of late-stage clinical failure due to toxicity. Liver organoids, in particular, are being studied extensively in drug toxicity evaluation, effectively reproducing the hepatotoxic characteristics of various compounds.⁵

Regarding personalized medicine and guiding cancer treatment, an increasing number of observational studies suggest that organoid drug sensitivity results can accurately

predict patient response to the same drug.⁴ The drugs assessed encompass a broad range of therapeutic agents, including cytotoxic chemotherapies, small-molecule targeted therapies, and biologics (e.g., antibodies and cellular therapies). Recognizing the heterogeneity of patient responses to the same drug, organoid drug sensitivity testing has the potential to enhance the accuracy of clinical medication selection and guide treatment decisions for patients resistant to standard regimens. Currently, many companies are commercializing organoid drug sensitivity testing.

Beyond the applications discussed above, organoids have demonstrated utility in additional fields. For example, organoid models are valuable tools for studying infectious diseases. The COVID-19 pandemic, which emerged in late 2019, highlighted the utility of lung organoids. Lung organoid models have been used to investigate the mechanisms of SARS-CoV-2 infection and to screen potential antiviral therapies. Traditional cell lines or animal models often prove inadequate for these tasks. Furthermore, in the areas of organ regeneration and tissue engineering, researchers are exploring the use of organoid technology for islet regeneration and diabetes therapy. Overall, organoids exhibit a broad range of applications and hold potential promise for advancing biomedical research across numerous disciplines.

Despite the considerable anticipation surrounding the translation of organoid technology into clinical practice and commercialization, this field faces several significant challenges. In basic research, the high cost of reagents and the complexity of three-dimensional culture limit widespread adoption of organoids in biomedical

laboratories. Therefore, the development of more efficient and affordable commercial organoid culture reagents and supporting equipment is crucial to facilitate the transition from traditional two-dimensional cell lines to organoid models. For drug discovery and development, the construction of high-quality, diverse organoid biobanks is essential. Biobanked organoids should be evaluated for robust passaging and cryopreservation, accompanied by systematic pathological, molecular, and genetic evaluation. To facilitate the translation of organoid drug testing into clinical practice, improvements in the standardization and automation of organoid culture and drug sensitivity testing are essential. Fortunately, many organizations and companies are working to promote the standardization of organoid culture and develop automated organoid culture devices.^{6,7}

Another limitation of organoids is their inability to fully replicate the tumor microenvironment, including crucial components such as immune cells, blood vessels, and stromal cells. Progress has been made to incorporate these microenvironmental factors and to develop complex co-culture systems.⁸ Furthermore, technological optimization is needed to improve culture success rates and reduce turnaround times for drug testing. Ultimately, validation of organoid drug test results through prospective interventional clinical trials is vital to generate robust clinical evidence and support clinical adoption.

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Author contributions

Conceptualization: Leping Yan

Visualization: Wei Chen

Writing—original draft: Wei Chen

Writing—review & editing: Leping Yan, Joaquim M. Oliveria, Rui L. Reis, Changhua Zhang, Yulong He

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