

Original Article



Patient-Derived Vs iPSC-Derived Organoids: Complementary Platforms for Translational and Regenerative Medicine

Muhamad Farid Zulkifle ^{1,*}, Roslina Husaini ², Norodiyah Othman ¹

¹ Cancer Research Centre (CaRC), Institute for Medical Research (IMR), National Institutes of Health (NIH), Ministry of Health (MOH), Bandar Setia Alam, Shah Alam, Selangor Darul Ehsan, Malaysia

² Centre for Coordination Clinical Research Networking (CCRN), Institute for Clinical Research (ICR), National Institutes of Health (NIH), Ministry of Health (MOH), Bandar Setia Alam, Shah Alam, Selangor Darul Ehsan, Malaysia

*Correspondence to: Muhamad Farid Zulkifle, Cancer Research Centre (CaRC), Institute for Medical Research (IMR), National Institutes of Health (NIH), Ministry of Health (MOH), Bandar Setia Alam, Shah Alam, Selangor Darul Ehsan, Malaysia. ORCID: <https://orcid.org/0000-0003-3425-7632>. Tel: +60 3 3362 7806, E-mail: zmfarid@moh.gov.my

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ABSTRACT

Three-dimensional (3D) organoid cultures have transformed the way researchers bridge the gap between conventional two-dimensional (2D) systems and living tissue. Here, we compare the two organoid platforms that now dominate biomedical research patient-derived organoids (PDOs) and induced pluripotent stem cell (iPSC)-derived organoids and consider how combining their strengths might shape the future of translational and regenerative medicine. PDOs retain a donor's genetic, histopathological and phenotypic features, which makes them well suited to rapid, clinically relevant modelling of cancer, infectious disease and fibrosis; their main drawbacks are limited tissue availability, dependence on animal-derived matrices, and an incomplete tumour microenvironment. iPSC-derived organoids, by contrast, can be expanded almost indefinitely and are readily amenable to genetic manipulation, making them attractive for developmental and rare disease research, although they tend to remain immature and are costly to produce. We review several emerging approaches that address these shared limitations co-culture and organoid-on-chip systems, multi-omics integration, and vascularised assembloids alongside the ethical and regulatory questions that both platforms raise. Rather than competing technologies, we argue that PDOs and iPSC-derived organoids are best treated as complementary tools, and that hybrid models combining patient specificity with scalability offer a promising way forward. We also discuss the limitations of this narrative review, including its non-systematic search strategy.

KEYWORDS

organoids, patient-derived organoids, induced pluripotent stem cells, disease modelling, precision medicine, regenerative medicine.

INTRODUCTION

Three-dimensional (3D) organoid models have transformed how researchers bridge the translational gap between conventional two-dimensional (2D) cultures and in vivo systems [1-3]. Grown from self-organising stem cells, organoids recapitulate key features of organ architecture and function, and have become powerful tools across basic research, disease modelling, and translational medicine [4-6,7].

Two platforms currently dominate the field. Patient-derived organoids (PDOs), are generated directly from adult stem cells isolated from patient tissues [8,9], while iPSC-derived or-

ganoids are established by reprogramming somatic cells into induced pluripotent stem cells (iPSCs) and then differentiating them into organ-specific structures [10-12]. Figure 1 provides a schematic overview of both systems and their main applications.

METHODS

This is a narrative rather than a systematic mini review, based on a search of the literature published up to September 2025. We identified relevant articles in PubMed, Scopus, and Web of Science using the terms "patient-derived organ-

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oids", "iPSC-derived organoids", "advantages", "limitations", "cancer modelling", and "translational research", giving preference to peer-reviewed studies, systematic reviews, and seminal papers offering comparative insights into the two platforms; further references were drawn from the bibliographies of these papers. Articles were screened for relevance, and the data extracted narratively to draw out the strengths, drawbacks, and emerging solutions associated with each approach. Because this is a narrative rather than a systematic review, it was not conducted against a pre-registered protocol or a formal quality appraisal framework, and reflects our own focused reading of the literature rather than exhaustive, reproducible search a point we return to as a limitation in the conclusion.

PATIENT-DERIVED ORGANOIDs: STRENGTHS AND CLINICAL RELEVANCE

Advantages of PDOs

Patient-derived organoids owe much of their growing popularity to how quickly they can be established. Cultures can typically be generated from patient tissue within a timeframe that is compatible with real world clinical decision-making [6,13], and because they retain the donor tumour's genetic alterations, histopathological organisation, and phenotypic heterogeneity, they tend to be strongly predictive of how a given patient will respond to chemotherapy or targeted therapy [5,9,10].

This fidelity extends down to the genetic and epigenetic level: PDOs preserve both intra- and inter-patient heterogeneity [8,9], which is precisely what makes them so useful for personalised medicine particularly in oncology, where drug sensitivity testing on patient's own organoids can help predict how they will respond to treatment (Table 1). The same direct derivation from patient tissue also underpins their strong translational fidelity in modelling cancer, gastrointestinal disorders, and cystic fibrosis [10-12,14].

Because PDOs are comparatively cheaper and less technically demanding to generate than iPSC-based systems, researchers have been able to build living organoid biobanks that serve as valuable resources for large-scale drug screening and biomarker discovery [9,13]. Oncology has benefited most from this approach: PDO libraries testing responses to chemotherapy and targeted agents now provide a functional bridge between a tumour's genomic profile and its actual treatment outcomes [9,15,16].

Oncology is not the only field to have benefited. PDOs and iPSC-derived organoid have also reshaped how infectious diseases and fibrotic disorders are modelled. Because PDOs preserve native tissue architecture, epithelial diversity and a donor's own genetic background, they can faithfully reproduce host pathogen interactions and the variability in infection severity seen between individuals; recent work has posi-

tioned organoids as essential tools for studying viral tropism, epithelial barrier function and antiviral responses in human tissue [17]. This has already uncovered physiological mechanisms such as mucin mediated restriction of coronavirus infection in the intestinal epithelium, and inflammatory macrophage activation within immune competent organoids infected with SARS-CoV2. iPSC-derived organoids complement this work by offering a scalable, genetically controlled system for studying host genetics and pathogen tissue interactions, and are increasingly used in antiviral drug screening [17].

Fibrosis modelling has grown alongside this. Intestinal and hepatic PDOs recapitulate patient-specific fibrotic processes such as epithelial mesenchymal transition, extracellular matrix deposition and fibroblast mediated remodelling, and fibroblast organised microenvironments have been shown to shape drug sensitivity within these PDO systems [8,12]. iPSC-derived organoids offer a similarity versatile platform: pluripotent stem cell-derived liver organoids have been used to model drug induced liver injury and screen for antifibrotic compounds, and iPSC-derived lung organoids provide a controllable system for studying how tissue injury drives extracellular matrix deposition and remodelling [12,18,19]. Taken together, the two platforms complement one another well across infectious disease and fibrosis research, supporting mechanistic discovery, personalised disease modelling and preclinical therapeutic testing.

Limitations of PDOs

These strengths come with real trade-offs. Establishing PDOs depends heavily dependent on the availability and quality of fresh patient material, and success rates vary considerably by tissue type and tumour subtype [1,20]. More fundamentally, PDOs lack much of the native tumour microenvironment, stromal, vascular, immune, and neural elements are all largely absent, which limits how well they can model systemic interactions [8,12,21,22].

Many protocols also still rely on animal-derived matrices such as Matrigel, which introduces batch to batch variability and its own ethical issues [12,23]. Expanding cultures over time carries a risk of clonal selection that can gradually erode the heterogeneity researchers are trying to preserve, and inconsistent protocols across laboratories continue to undermine reproducibility [1,10]. Patient consent, data privacy, and equitable access to biobanks add a further layer of complexity to clinical adoption [24]; we return to these governance issues later (see Ethical and Translational Considerations).

IPSC-DERIVED ORGANOIDs: VERSATILITY AND GENETIC TRACTABILITY

Advantages of iPSC-derived Organoids

iPSC-derived organoids offer a different, and largely complementary, set of strengths. They can be generated from easily

accessible sources such as skin fibroblasts or peripheral blood, reprogrammed into a pluripotent state, and then differentiated into a wide range of tissue lineages [4,25,26]. Because the resulting lines are renewable, they can be expanded indefinitely, supporting large-scale, reproducible experiments in a way PDOs generally cannot.

This scalability is a genuine advantage: because iPSCs can, in principle, be generated from anyone, organoids can be established even when a patient biopsy simply is not available, a real benefit for studying developmental disorders and rare diseases [24,28,42]. Their developmental plasticity also makes them well suited to studying organogenesis directly, and genome editing tools such as CRISPR/Cas9 allow researchers to build isogenic models that help tease apart genotype-phenotype relationships [9,13].

Beyond disease modelling, this same genetic tractability has made iPSC-derived organoids particularly valuable in developmental biology and regenerative medicine, offering an unprecedented window into human organogenesis and real promise for future cell-based therapies [9,25].

Limitations of iPSC-derived Organoids

These advantages come at a cost. The biggest challenge is immaturity: iPSC-derived organoids often resemble foetal rather than adult tissues [20,26], which limits their usefulness modelling late-onset diseases or drug responses. Producing them is also slow and labour-intensive, often taking more than six weeks of culture before reaching functional maturity [4,9,26].

Genetic instability introduced during reprogramming and extended culture is a further concern, particularly around tumorigenic potential in any future clinical use [11,25]. Differentiation protocols can take months and still yield variable results, and residual epigenetic memory or incomplete differentiation can introduce artefacts that complicate interpretation of the data.

High costs and the need for specialised expertise have also slowed broader uptake relative to PDOs [8,20], and, as with PDOs, the lack of stromal, vascular, and immune components still limits how physiologically accurate these models can be [11,15].

Comparison of PDOs vs iPSC-derived Organoids: Advantages, Disadvantages, and Solutions

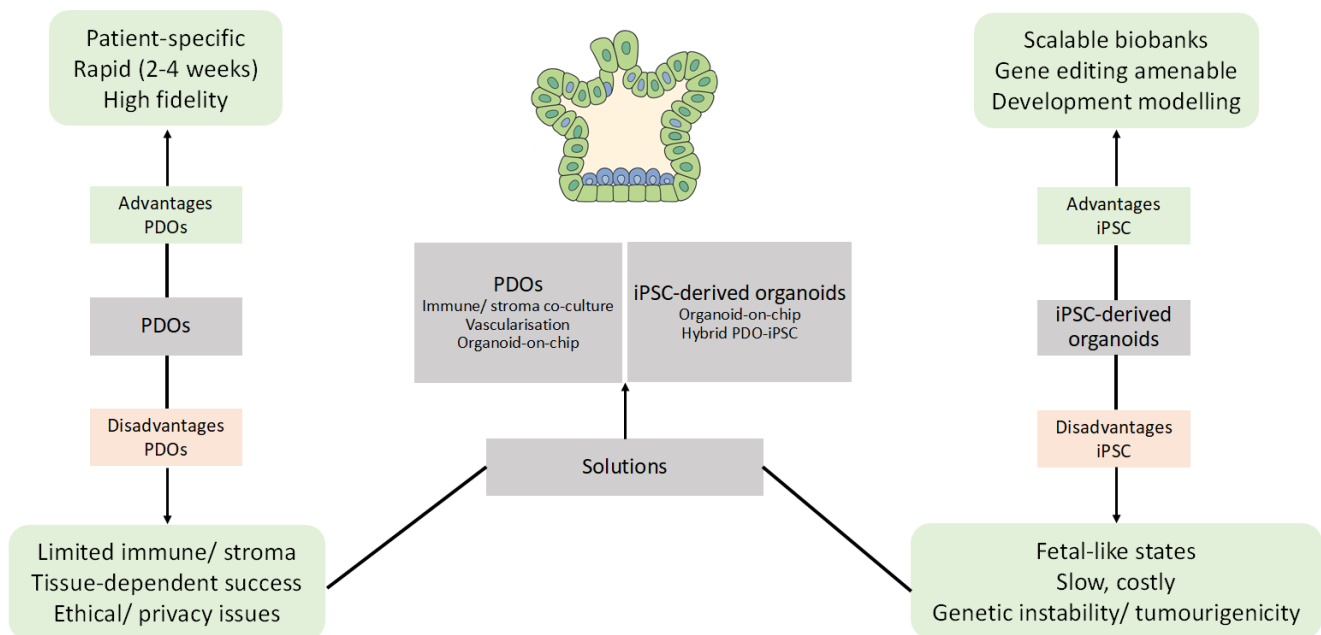


Figure 1. Overview of organoid systems. Schematic representation of the two main organoid platforms: patient-derived organoids (PDOs), established directly from patient biopsy or surgical material, and iPSC-derived organoids, generated by reprogramming somatic cells into induced pluripotent stem cells (iPSCs) and differentiating them into organ-specific models. Key applications, including disease modelling, drug screening, and regenerative medicine, are indicated.

In this mini review, we compare the relative strengths and limitations of these two platforms, highlight emerging strategies that address their shortcomings, and consider how bringing them together might shape the future of biomedical research and clinical translation.

Maturation Strategies for iPSC-derived Tissues: 3D Bioprinting, Hypoxia, and Co-culture Approaches

Given how much this immaturity limits their usefulness for modelling late-stage physiology, drug responses and complex disease, researchers have developed several strategies aimed at pushing iPSC-derived tissues towards greater structural organisation and functional maturity.

Three dimensional (3D) bioprinting is one of the more promising of these approaches, since it gives researchers precise spatial control over where cells are placed and how the extracellular matrix is arranged. Building constructs layer by layer from cell laden bioinks produces a hierarchical, tissue like geometry that self-organising spheroids and simple aggregates cannot easily replicate. Tuneable bioinks and scaffolds designs can be used to influence mechanical properties and biochemical signalling, which in turn helps guide lineage progression in cardiac, hepatic and neural constructs [27], and incorporating supportive hydrogels and patterned channels improve nutrient and oxygen diffusion, reducing central necrosis and encouraging a more native like multicellular organisation.

Oxygen tension is another factor that is often overlooked. physiological tissues experience far lower oxygen levels than the atmospheric conditions used in most culture systems and controlled hypoxic or physioxic culture can activate hypoxia-inducible pathways that regulate angiogenic, metabolic and differentiation networks, nudging iPSC-derived cells towards more mature phenotypes. Formal hypoxia conditioning studies in iPSC organoids are still relatively rare, but the wider tissue engineering literature is fairly consistent on the value of tuning oxygen gradients in 3D constructs, both to prevent central necrosis and to better mimic the developmental niches these cells would encounter in vivo; the same gradients can also drive regional patterning that resembles native organ histology.

Co-culture is arguably just as important. In native tissue, epithelial, stromal, endothelial, immune and neural cells interact

constantly through direct contact and paracrine signalling to regulate development, homeostasis and repair, and recreating even part of that complexity in vitro noticeably improves iPSC-derived tissue maturity. Co-culturing iPSC-derived cardiomyocytes with endothelial cells and stromal populations within 3D hydrogels, for example, improves contractile function and shifts gene expression closer to that of adult myocardium. These multicellular environments also support vascularisation, improving nutrient delivery and waste removal, and provide the mechanical and biochemical cues that drive organ specific maturation. Adding supporting cell types such as fibroblasts or mesenchymal cells contributes further extracellular matrix cues that refine tissue organisation and resilience, and when combined with advanced matrix platforms, these systems can produce functional readouts, electrophysiological maturation in cardiac constructs, metabolic competence in hepatic tissues, barrier formation in epithelial models that are difficult to achieve in monoculture.

None of these approaches is mutually exclusive, and it is likely that combining engineered microarchitecture, oxygen tuned microenvironments and supportive co-culture will do more for iPSC-derived tissue maturity than any one strategy alone and, in doing so, make these models more useful for disease modelling, drug screening and regenerative medicine.

COMPARATIVE ANALYSIS AND APPLICATIONS

Taken together, this evidence points to a simple conclusion: PDO and iPSC-derived organoids work best as complementary tools rather than rival technologies. PDOs are hard to beat in translational oncology, where speed and patient specificity matter most for informing treatment decisions [9,13], while iPSC-derived organoids are better suited to fundamental biology, regenerative medicine and the mechanistic dissection of genetic disease [9,26]. Table 1 and Figure 2 summarise how these different strengths map onto different priorities.

Table 1. Comparative advantages and limitations of PDCOs and iPSC-derived organoids

Feature	PDOs	iPSC-derived organoids
Establishment time	2-4 weeks	6-12+ weeks
Patient fidelity	High – preserves patient genetics/ pheno-type	Variable – depends on reprogramming fidelity
Scalability	Limited by tissue availability	Unlimited from reprogrammed cells
Genetic manipulation	Limited	Highly amenable to CRISPR/ Cas9 editing
Maturity	Adult-like characteristics	Often foetal-like phenotypes
Cost	Moderate	High (labour- and expertise- intensive)
Clinical translation	Rapid turnaround for precision medicine	Slower but suitable for regenerative applications

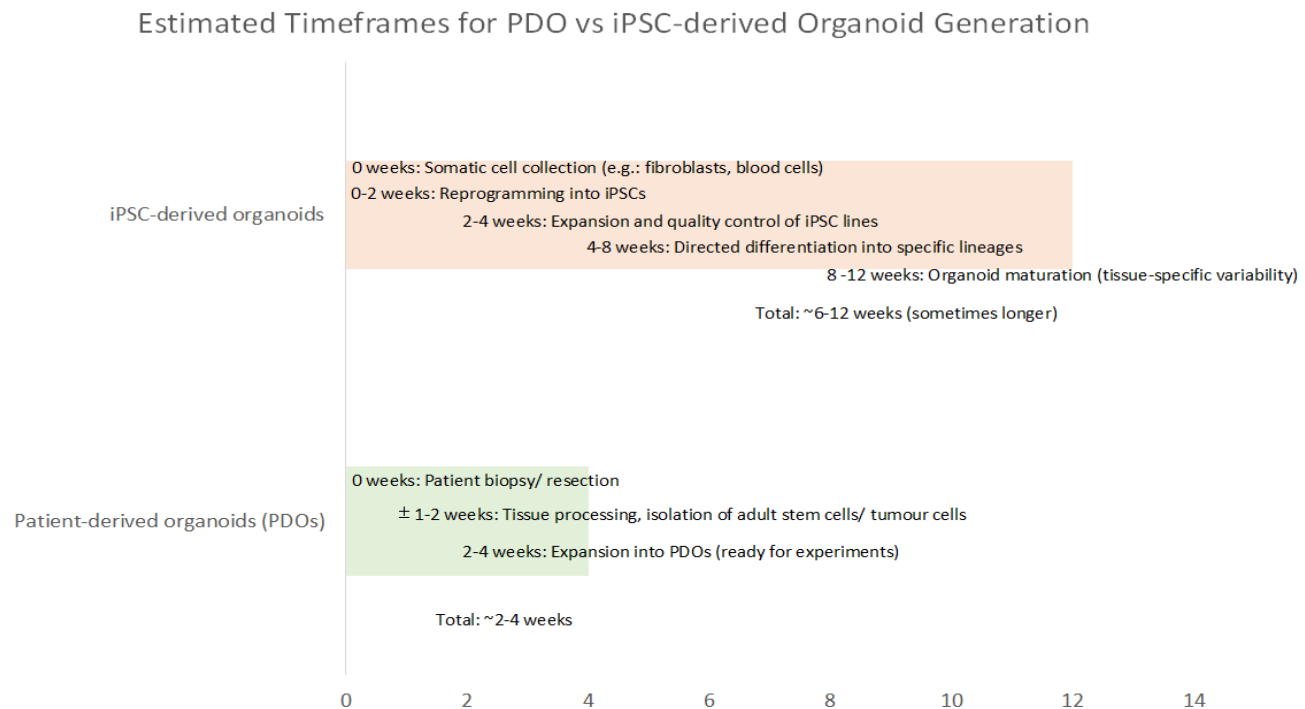


Figure 2. Comparative advantages and limitations of PDOs and iPSC-derived organoids. Summary of the major strengths and drawbacks of each organoid system. PDOs are highlighted for their rapid establishment and faithful recapitulation of tumour heterogeneity, whilst iPSC-derived organoids are emphasised for their scalability and genetic tractability. Shared challenges, including lack of immune, stromal, and vascular components, are illustrated.

Beyond these broad comparisons, the two platforms also diverge in how they are actually applied across research and clinical settings, as summarised in Table 2. PDOs, for instance, have shown roughly 80-90% clinical concordance in predicting chemotherapy response in metastatic colorectal cancer (CRC) [21,29], while CRISPR-corrected iPSC-derived organoids have achieved substantial in some models over 70%, phenotypic correction in rare monogenic disease [20,26,30]. These figures vary by disease and correction strategy and should be checked against the primary source before submission.

Table 2. Applications of PDOs and iPSC-derived organoids in research and clinical translation

Application area	PDOs	iPSC-derived organoids
Cancer research	Patient-specific tumour modelling; drug response prediction; biobanks for high-throughput screening (~80-90% clinical concordance reported in colorectal cancer (CRC); [9,21,29].	Modelling cancer initiation from defined mutations via CRISPR/ Cas9; studying tumourigenesis in developmental contexts [22,31, 32].
Drug discovery and toxicology	Functional precision medicine; preclinical drug efficacy testing; biomarker identification [25,33,34].	Large scale compound screening; modelling patient diversity through iPSC cohorts [12,18,24].
Genetic diseases	Limited utility, but possible when derived from affected tissues (e.g.: cystic fibrosis PDO); [14,16].	Broad utility in modelling hereditary disorders (e.g.: lissencephaly, retinal degeneration); CRISPR-corrected models showing substantial phenotypic rescue [20,26,30].
Developmental biology	Limited ability to study embryogenesis (derived from adult stem cells).	Powerful models for organogenesis, neuronal and intestinal development [13,24,27].
Regenerative medicine	Currently exploratory; transplantation potential under investigation [19,31].	High promise for tissue engineering and regenerative therapy (e.g.: liver buds, cortical grafts); [18,19,31,32].

Table 3. Emerging solutions to overcome platform-specific limitations

Challenge	PDOs	iPSC-derived organoids	Shared solutions	Stage of validation
Microenvironment	Co-culture with patient matched immune/ stromal cells	Integration with engineered tissue scaffold	Organoid-on-chip systems; bioprinting	Pre-clinical
Scalability	Standardised biobanking protocols	Automated culture system	High-throughput platforms	Pre-clinical–early clinical
Maturation	N/A (already mature)	Extended culture protocols; metabolic cues	Mechanical stimulation	Pre-clinical
Reproducibility	Protocol standardisation	Quality control metrics	Machine learning guided assessment	Pre-clinical
Vascularisation	Endothelial/ vascular co-culture in tumour PDOs	Vascularised assembloids; microfluidic perfusion	Organ-on-chip (OOAC) systems	Pre-clinical

EMERGING SOLUTIONS AND FUTURE DIRECTIONS

Addressing Common Limitations

PDOs and iPSC-derived organoids share several challenges, and researchers are tackling them through a range of innovative approaches. Chief among these is the absence of immune, stromal, and vascular components, which is now being addressed through the strategies summarised in Table 3. For PDOs, this has meant integrating synthetic biomaterials, co-culturing with autologous immune cells, and using organoid-on-chip systems to better approximate physiological conditions [3,8,21]. For iPSC-derived organoids, protocols are being refined to improve maturation through longer culture periods, engineered scaffolds, and vascularisation via endothelial co-culture [32,35].

Newer co-culture models incorporating T cells, macrophages, and fibroblasts are starting to close this microenvironment gap, making it possible to study immune tumour interactions and immunotherapy responses directly [3,22,24,36,42]. Organoid-on-chip platforms and bioprinting methods are similarly being developed to build in vascular networks, which allows larger, more physiologically realistic structures to be cultured [8,21,37].

Technological Innovations

Computational tools are playing a growing role here too deep learning based morphological assessment, for example, is helping to improve quality control and reduce variability between organoid lines [18,31,32,35,38,39]. Often efforts include using metabolic and mechanical cues to promote maturation, automating culture and imaging to improve reproducibility, and introducing microfluidic systems to support vascularisation and perfusion [9,16].

Integration Strategies

Hybrid approaches are, in our view, one of the more exciting directions for the field. Combining patient-derived genetic material with iPSC platforms could, in principle, merge translational fidelity with scalability, addressing the limitations of

each approach individually [1,34,40,41]. One example already under active investigation is the PDO-seeded iPSC-derived scaffold, in which patient tumour or tissue cells are combined with a scalable, genetically tractable iPSC-derived structural framework for regenerative or disease modelling use, the aim being to combine patient specific fidelity with the reproducibility of an iPSC platform. These hybrid systems raise their own ethical and ownership questions, though: who holds rights over a construct built from both a patient's tissue and a reprogrammed cell line? How should consent be structured if the construct is later used commercially? And how should biobank governance apply once patient- and donor-derived materials are combined within a single model? These are questions that will need to be worked through alongside the technical development of hybrid platforms.

Next-generation Advances

A handful for converging technologies look set to shape the next generation of organoid research.

Multi-omics integration

Multi-omics integration has substantially sharpened the resolution of both PDOs and iPSC-derived organoids as experimental and translational platforms. In PDOs, it allows investigators to capture the molecular landscape of an individual tumour by linking genomic alterations to transcriptomic, proteomic and metabolic states uncovering patient specific vulnerabilities that more limited assays would miss; this works precisely because PDOs retain the genetic heterogeneity, mutational profile and functional responses of the original tumour, making them powerful avatars for precision oncology [21,37]. iPSC-derived organoids offer a different advantage here a genetically controlled system, free from tumour associated confounders, in which multi-omics can instead be used to study normal tissue development, differentiation trajectories and disease mechanisms. Single cell multi-omics applied across both platforms has already shed light on differentiation hierarchies, rare cell subpopulations and the transcrip-

tional dynamics underlying lineage trajectories and cell state transitions, and combining this with epigenomic profiling helps to map the regulatory networks driving differentiation and disease phenotypes; proteomic and metabolomic layers then add a further dimension of functional depth not always visible at the RNA level. Challenges remain on both sides, however PDOs are prone to culture induced drift and selection pressure that requires careful computational correction, while iPSC-derived organoids often show enough variability in differentiation efficiency to complicate downstream data interpretation.

Artificial intelligence (AI)-assisted maturation and analysis

Artificial intelligence (AI) has moved quickly from a peripheral tool a genuine driver of innovation in both PDO and iPSC-derived organoid research, improving maturation, standardisation and high throughput analysis [38,39]. In PDOs, AI-enabled platforms can automatically analyse time lapse or high content microscopy image to quantify morphology, budding, lumen formation, cell death and growth kinetics, moving well beyond simple endpoint viability assays and providing richer, real-time data on drug response. This kind of imaging-based phenotyping speeds up throughput and reduces subjectivity, which in turn allows more consistent quality control across diverse PDO lines. In iPSC-derived organoids, AI is proving particularly useful for guiding differentiation: machine learning (ML) models can read early morphological cues, predict differentiation outcomes, and adjust culture conditions (e.g.: media, growth factors, ECM conditions) in real time to steer maturation more reliably [38,39]. Multimodal frameworks that integrate imaging data with multi omics readouts (transcriptomic, proteomic, metabolomic) and functional assays are also starting to emerge for both platforms, allowing organoid state, lineage composition or drug sensitivity to be predicted without destructive assays, preserving scarce patient-derived material while still maximising the data obtain from it. Real challenges remain, though: AI models need large, diverse training datasets to avoid bias, imaging conditions, and culture protocols still vary considerably between laboratories, and clinical translation will demand a level of reproducibility, interpretability and validation that the field has not yet fully established.

Vascularised assembloids

Vascularised assembloids are arguably one of the biggest steps forward in organoid engineering, since they allow functional endothelial networks to be built into both PDO-based and iPSC-derived systems [37]. Standard organoids, whatever their origin, typically lack vasculature, which becomes a real problem once they grow beyond a certain size: nutrient, oxygen and waste exchange breaks down, and central hy-

poxia, necrosis, or restricted maturation follow. Researchers have addressed this in several ways, co-culturing with endothelial progenitor cells, using microfluidic perfusion in organ-on-a-chip (OOAC), bioprinting vascular channels, or implant constructs in vivo to produce perfusable three-dimensional (3D) constructs with improved viability, maturation and structural complexity [37]. In tumour-derived PDO assembloids, the resulting vascular networks make it possible to model the tumour microenvironment far more realistically, capturing tumour endothelial interactions, angiogenesis, stromal cross-talk and drug penetration dynamics that matter enormously for studying metastasis, drug delivery and therapy resistance [37]. In iPSC-derived organoids, vascularisation supports more advanced tissue maturation and allows developmental processes that depend on endothelial interplay or perfusion to be studied directly, pushing these models beyond early development towards something closer to adult tissue. None of this is straightforward, though: standardising endothelial cell sources, extracellular matrix composition, and perfusion parameters remains technically demanding, particularly at medium- to high-throughput scale [37]. Even so, vascularised assembloids represent a genuinely more physiological stage in organoid technology, and one that considerably broadens what both platforms can be used for.

ETHICAL AND TRANSLATIONAL CONSIDERATIONS

The ethical questions raised by organoid research differ somewhat between the two platforms, and both sets of questions have grown more pressing as PDOs and iPSC-derived organoids closer to clinical use.

For iPSC-derived organoids, relying less on patient tissue does not make the ethics any simpler. Reprogramming raises its own questions about the scope of the original consent, particularly where cell lines end up being banked and reused for purposes nobody anticipated at the time of collection; about the long-term genomic stability of reprogrammed lines; and about equitable access to whatever regenerative therapies eventually result [34]. A concern that has gained more attention recently is equity in biobanking. Most large iPSC repositories and reference panels have been built predominantly from individuals of European and East Asian ancestry, which means genetic and disease modelling insights may not generalise well to underrepresented populations, and that the benefits of any resulting therapeutics could end up distributed quite unevenly across regions and ethnic groups. Diversifying the ancestral and geographic reach of iPSC biobanks is therefore as much an ethical priority as a scientific one.

PDOs raise a different, though related, set of governance issues, given how directly they depend on sensitive patient tissue and clinical data [24]. Central among these are how far, and for how long, consent for biobank tissue use should ex-

tend including to future research that was never specified at the time of collection along with the protection of patient privacy, since PDOs and their derived omics data are inherently re-identifiable. There is also the question of what regulatory pathway is needed to move a PDO-based diagnostic or drug-sensitivity assay out of the research setting into accredited clinical decision making. Regulation here has not kept pace with the science: frameworks for PDO-based companion diagnostics remain underdeveloped, and validation standards will need to be harmonised across jurisdictions before PDO guided treatment selection can be adopted more widely. Both platforms, finally, raise questions of ownership and commercialisation, especially as hybrid PDO–lpsc systems and biobank-derived cell lines are increasingly licensed out for industrial drug screening. Addressing this will take coordinated standardisation across research institutions and genuinely transparent biobank governance without which reproducibility and equitable access will both suffer [1,20].

CONCLUSION

PDOs and iPSC-derived organoids each bring something distinct to the study human biology and disease. PDOs offer rapid, clinically relevant models that preserve patient's own biology, which is what makes them so valuable for precision medicine. iPSC-derived organoids take longer and are more technically demanding to establish, but offer scalability, genetic tractability and versatility that PDOs simply cannot match, particularly for developmental and regenerative work. Both systems still struggle to recreate the full complexity of the human tissue microenvironment, but recent advances in co-culture systems, organoid-on-chip technologies, vascularisation, multi-omics integration, AI-assisted analysis, and automation are starting to close that gap. The field, as a whole, seems to be moving towards integrative models that draw on the strengths of both platforms while addressing their weakness through engineering, computational and ethical innovation in parallel. Hybrid models that combine patient specificity with scalability, backed by continued technological progress and appropriate ethical frameworks, may well represent the next stage of organoid technology and, with it, new possibilities for understanding human disease and developing more effective treatments.

A few limitations of this review are worth flagging. As a narrative rather than systematic review, it does not follow a pre-registered protocol or a formal risk of bias assessment, nor does it draw on an exhaustive database search, so the literature discussed here is subject to a degree of selection bias. The search itself was restricted to English-language, peer-reviewed sources in PubMed, Scopus, and Web of Science (WoS), which may have excluded relevant regional or non-English work. Because the field is moving quickly, some of the technologies covered here AI-assisted analysis and vas-

cularised assembloid engineering in particular are still represented mainly by early stage of pre-clinical studies, and it remains to be seen how much clinical impact they will ultimately have. Finally, the quantitative comparisons in Table 2, such as the clinical concordance and phenotypic correction rates quoted above, come from specific disease contexts and study designs, and should not be generalised across all organoid applications without checking the primary literature.

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Conflicts of Interest

The authors have no conflict of interest to declare

REFERENCES

- [1] Lancaster MA, Knoblich JA. Organogenesis in a dish: modelling development and disease using organoid technologies. *Science*. 2014;345(6194):1247125.
- [2] Clevers H. Modeling development and disease with organoids. *Cell*. 2016;165(7):1586–97.
- [3] Fatehullah A, Tan SH, Barker N. Organoids as an in vitro model of human development and disease. *Nat Cell Biol*. 2016;18(3):246–54.
- [4] Huch M, Koo BK. Modeling mouse and human development using organoid cultures. *Development*. 2015;142(18):3113–25.
- [5] Yin X, Mead BE, Safaee H, Langer R, Karp JM, Levy O. Engineering stem cell organoids. *Cell Stem Cell*. 2016;18(1):25–38.
- [6] Rossi G, Manfrin A, Lutolf MP. Progress and potential in organoid research. *Nat Rev Genet*. 2018;19(11):671–87.
- [7] Ahammed B, Kalangi SK. A decade of organoid research: progress and challenges in the field of organoid technology. *ACS Omega*. 2024;9(28):30087–96. doi:10.1021/acsomega.4c03683.
- [8] Sato T, Stange DE, Ferrante M, Vries RGJ, Van Es JH, Van den Brink S, et al. Long-term expansion of epithelial organoids from human colon, adenoma, adenocarcinoma, and Barrett's epithelium. *Gastroenterology*. 2011;141(5):1762–72.
- [9] Vlachogiannis G, Hedayat S, Vatsiou A, Jamin Y, Fernández-Mateos J, Khan K, et al. Patient-derived organoids model treatment response of metastatic gastrointestinal cancers. *Science*. 2018;359(6378):920–6.
- [10] Takahashi K, Yamanaka S. Induction of pluripotent stem cells from mouse embryonic and adult fibroblast cultures by defined factors. *Cell*. 2006;126(4):663–76.
- [11] Eiraku M, Takata N, Ishibashi H, Kawada M, Sakakura

- E, Okuda S, et al. Self-organizing optic-cup morphogenesis in three-dimensional culture. *Nature*. 2011;472(7341):51–6.
- [12] McCauley HA, Wells JM. Pluripotent stem cell-derived organoids: using principles of developmental biology to grow human tissues in a dish. *Development*. 2017;144(6):958–62.
- [13] Paşca AM, Sloan SA, Clarke LE, Tian Y, Makinson CD, Huber N, et al. Functional cortical neurons and astrocytes from human pluripotent stem cells in 3D culture. *Nat Methods*. 2015;12(7):671–8.
- [14] de Poel E, Spelier S, Hagemeijer MC, van Mourik P, Suen SWF, Vonk AM, et al. FDA-approved drug screening in patient-derived organoids demonstrates potential of drug repurposing for rare cystic fibrosis genotypes. *J Cyst Fibros*. 2023;22(3):548–59. doi:10.1016/j.jcf.2023.03.004.
- [15] Kim M, Mun H, Sung CO, Cho EJ, Jeon HJ, Chun SM, et al. Patient-derived lung cancer organoids as in vitro cancer models for therapeutic screening. *Nat Commun*. 2019;10(1):3991.
- [16] Schutgens F, Clevers H. Human organoids: tools for understanding biology and treating diseases. *Annu Rev Pathol*. 2020;15:211–34.
- [17] Chu JTS, Lamers MM. Organoids in virology. *npj Viruses*. 2024;2:2. doi:10.1038/s44298-024-00017-5.
- [18] Dye BR, Hill DR, Ferguson MAH, Tsai YH, Nagy MS, Dyal R, et al. In vitro generation of human pluripotent stem cell-derived lung organoids. *eLife*. 2015;4:e05098.
- [19] Kim Y, Kang M, Mamo MG, Adisasmita M, Huch M, Choi D. Liver organoids: current advances and future applications for hepatology. *Clin Mol Hepatol*. 2025. doi:10.3350/cmh.2024.1040.
- [20] Bershteyn M, Nowakowski TJ, Pollen AA, Di Lullo E, Nene A, Wynshaw-Boris A, et al. Human iPSC-derived cerebral organoids model cellular features of lissencephaly and reveal prolonged mitosis of outer radial glial. *Nat Cell Biol*. 2017;19(6):568–76.
- [21] Ooft SN, Weeber F, Dijkstra KK, McLean CM, Kaing S, van Werkhoven E, et al. Patient-derived organoids can predict response to chemotherapy in metastatic colorectal cancer patients. *Sci Transl Med*. 2019;11(513):eaay2574.
- [22] Polak R, Zhang ET, Kuo CJ. Cancer organoids 2.0: modelling the complexity of the tumour immune micro-environment. *Nat Rev Cancer*. 2024;24(8):523–39. doi:10.1038/s41568-024-00706-6.
- [23] Weeber F, van de Wetering M, Hoogstraat M, Dijkstra KK, Krijgsman O, Kuilman T, et al. Preserved genetic diversity in organoids cultured from biopsies of human colorectal cancer metastases. *Proc Natl Acad Sci U S A*. 2015;112(43):13308–11.
- [24] Lancaster MA, Renner M, Martin CA, Wenzel D, Bicknell LS, Hurles ME, et al. Cerebral organoids model human brain development and microcephaly. *Nature*. 2013;501(7467):373–9.
- [25] Sachs N, Clevers H. Organoid cultures for the analysis of cancer phenotypes. *Curr Opin Genet Dev*. 2014;24:68–73.
- [26] Spence JR, Mayhew CN, Rankin SA, Kuhar MF, Vallance JE, Tolle K, et al. Directed differentiation of human pluripotent stem cells into intestinal tissue in vitro. *Nature*. 2011;470(7332):105–9.
- [27] Aili Y, Maimaitiming N, Wang Z, Wang Y. Brain organoids: a new tool for modelling of neurodevelopmental disorders. *J Cell Mol Med*. 2024;28(17):e18560. doi:10.1111/jcmm.18560.
- [28] Li Z, Li K, Zhang C, Zhao Y, Guo Y, He J, Chang S, Fang X, Liu K, Zhu P, Chen Z, Ruan C. Bioprinted organoids: an innovative engine in biomedicine. *Adv Sci (Weinh)*. 2025;12(33):e07317. doi:10.1002/advs.202507317.
- [29] Smabers LP, Wensink E, Verissimo CS, Koedoot E, Pitsa KC, Huismans MA, et al. Organoids as a biomarker for personalized treatment in metastatic colorectal cancer: drug screen optimization and correlation with patient response. *J Exp Clin Cancer Res*. 2024;43(1):1–16. doi:10.1186/s13046-024-02980-6.
- [30] Lim SW, Fang X, Cui S, Lee H, Shin YJ, Ko EJ, et al. CRISPR-Cas9-mediated correction of SLC12A3 gene mutation rescues the Gitelman's disease phenotype in a patient-derived kidney organoid system. *Int J Mol Sci*. 2023;24(3):3019. doi:10.3390/ijms24033019.
- [31] Huch M, Gehart H, van Boxtel R, Hamer K, Blokzijl F, Verstegen MMA, et al. Long-term culture of genome-stable bipotent stem cells from adult human liver. *Cell*. 2015;160(1–2):299–312.
- [32] Kadosh E, Snir-Alkalay I, Venkatachalam A, May S, Lasry A, Elyada E, et al. The gut microbiome switches mutant p53 from tumour-suppressive to oncogenic. *Nature*. 2020;586(7827):133–8.
- [33] Drost J, Clevers H. Organoids in cancer research. *Nat Rev Cancer*. 2018;18(7):407–418.
- [34] Yan HHN, Siu HC, Law S, Ho SL, Yue SSK, Tsui WY, et al. A comprehensive human gastric cancer organoid biobank captures tumour subtype heterogeneity and enables therapeutic screening. *Cell Stem Cell*. 2018;23(6):882–97.e11.
- [35] Kim J, Koo BK, & Knoblich JA. Human organoids: model systems for human biology and medicine. *Nat Rev Mol Cell Biol*. 2020;21:571–584.
- [36] Suhito IR, Sunil C, Tay A. Engineering human immune organoids for translational immunology. *Bioact Mater*. 2025;44:164–83. doi:10.1016/j.bioactmat.2024.10.010.
- [37] Zhou R, Brislinger D, Fuchs J, Lyons A, Langthaler S,

- Hauser CAE, Baumgartner C. Vascularised organoids: recent advances and applications in cancer research. *Clin Transl Med*. 2025;15(3):e70258. doi:10.1002/ctm2.70258.
- [38] Bai L, Wu Y, Li G, Zhang W, Zhang H, Su J. AI-enabled organoids: construction, analysis, and application. *Bioact Mater*. 2024;31:525–48. doi:10.1016/j.bioactmat.2023.09.005.
- [39] Maramraju S, Kowalczewski A, Kaza A, et al. AI-organoid integrated systems for biomedical studies and applications. *Bioeng Transl Med*. 2024;9(2):e10641. doi:10.1002/btm2.10641.
- [40] Tuveson D, Clevers H. Cancer modeling meets human organoid technology. *Science*. 2019;364(6444):952–955.
- [41] Corrò C, Novellademunt L, Li VSW. A brief history of organoids. *Am J Physiol Cell Physiol*. 2020;319(1):C151–65.
- [42] Quadrato G, Brown J, & Arlotta P. The promises and challenges of human brain organoids as models of neuropsychiatric disease. *Nat Med*. 2016;22(11):1220–8.