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Expert consensus on the establishment and clinical application of patient-derived endometrial cancer organoids

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ABSTRACT

Endometrial cancer (EC), the second most common gynaecologic malignancy, faces challenges in precision treatment due to limited predictive models for therapy selection. Patient-derived organoids, which recapitulate tumour heterogeneity and microenvironment, offer a transformative platform for drug sensitivity testing and personalised therapy. However, standardised protocols for establishing EC organoids, biobanking and clinical translation remain lacking consensus. This expert consensus proposes guidelines for EC organoid culture optimisation, characterisation and clinical validation. By harmonising technological advances with clinical needs, this consensus aims to accelerate the integration of organoid models into EC precision medicine, ultimately improving therapeutic outcomes.

BACKGROUND

Endometrial cancer (EC), an epithelial malignancy originating from the endometrium, ranks as the second most common gynaecologic malignancy, accounting for 20%–30% of all gynaecologic malignancies. China has exhibited a persistent rise in EC incidence since 2000, with newly diagnosed cases reaching 77 700 in 2022 and associated mortality totalling 13 500 during the same period.[1] Conventional management of EC primarily relies on surgery with adjuvant radiotherapy and/or chemotherapy. While advanced tumours with microsatellite instability-high (MSI-H) subtypes exhibit objective response rates of 40%–57.1% to immune checkpoint inhibitors,[2–5] effective targeted therapies remain limited for most advanced/recurrent cases beyond this subgroup. Consequently, patients typically receive conventional chemoradiotherapy with suboptimal outcomes, reflected in poor prognoses (5-year survival rate of ~20% for stage IV disease). Even in conservatively managed early-stage disease where complete remission rates exceed 75%, recurrence rates reach 40.6%,[6] underscoring a significant gap towards achieving precision oncology objectives. Current precision drug screening approaches include tumour genomic profiling for target identification and patient-derived xenograft models for empirical drug evaluation.[7] However, these methods face substantial limitations including high costs, prolonged timelines and significant ethical concerns associated with large-scale sacrifice of experimental animals during in vivo screening.

A seminal breakthrough in organoid technology occurred in 2009 when Hans Clevers' team successfully cultured small intestinal organoids. Recent years have witnessed rapid advancement of this technology in modelling cancer biology. Building on stem cell techniques, organoids develop through self-organisation of progenitor cells into sophisticated three-dimensional in vitro assemblies.[8] These structures faithfully replicate both the gene expression profiles and critical functional properties of corresponding organs, thereby achieving high architectural fidelity to native tissues. Additional advantages include short culture cycles, stable passaging and reliable cryopreservation with efficient recovery.[8–12] These combined attributes establish patient-derived tumour organoids (PDOs) as highly promising models for contemporary anti-cancer drug discovery and personalised therapeutic screening.

Turco *et al* pioneered the establishment of EC organoids (ECOs), providing a transformative model for studying endometrial carcinogenesis.[13] While demonstrating significant potential in clinical personalised therapeutics and biomedical development, ECOs remain in the exploratory phase, with standardisation gaps persisting in model construction guidelines, biobanking criteria and clinical drug screening protocols. Consequently, the Expert Committee of Obstetrics

and Gynaecology of the Chinese Research Hospital Association and the Chinese Society for Cell Biology have convened a multidisciplinary panel of experts in EC clinical practice and organoid research. Grounded in comprehensive analysis of global evidence, this consensus establishes guidelines to standardise ECOs modelling, accelerate clinical translation and optimise precision diagnostic-therapeutic strategies, thereby bridging the gap between cutting-edge organoid technology and clinical practice.

Standardised establishment of ECOs

Establishment protocols for ECOs are now technically feasible, with models successfully generated across key pathological subtypes including endometrioid carcinoma, serous carcinoma, clear cell carcinoma and carcinosarcoma.[14–16] Successful establishment of ECOs involves multistep protocols under stringent conditions, with reported maximum construction success rates of 91.6%.[14 17–19] Furthermore, organoid models derived from normal endometrium serve as robust in vitro platforms for investigating carcinogenic mechanisms such as driver gene functions and microenvironment remodelling.[13 18 20] Critical determinants of successful ECOs culture include: sample processing expertise, matrix selection and culture optimisation, as well tumour stage and histopathological characteristics.[17 21]

Procurement and transport of patient-derived tumour tissues

Regulatory compliance and ethical governance

As organoids constitute human genetic resources, their development and application must comply with China's Biosecurity Law and Regulations on Human Genetic Resources Management to safeguard national health, public interests and biosecurity. Prior to sample collection/storage, written informed consent addressing privacy protection and clinical usage must be obtained. The consent process explicitly covered the use of surgical specimens for ECO establishment, subsequent biomedical research, genomic analysis and the potential sharing of anonymised data in public repositories. To protect patient privacy, all samples and clinical data were de-identified using a unique coding system, with the encryption key stored separately under strict access control. All preclinical studies and clinical trials involving organoid drug sensitivity testing require ethical committee approval.[22]

Organisation acquisition and transportation

The successful establishment of ECOs necessitates precise sampling of tumour tissues with histopathological validation, coupled with strict aseptic conditions throughout processing and cryopreservation to maximise cellular viability. Importantly, organoid generation protocols must be designed to avoid interference with standard clinical diagnostic procedures or therapeutic interventions.

1. Specimen acquisition and handling: EC tissues should be procured from surgical resection or biopsy procedures using sterilised surgical instruments. During tumour dissection, areas exhibiting macroscopic necrosis or non-neoplastic components must be rigorously avoided. The minimum recommended tissue volume is 5 mm^3, with immediate transfer into sterile transport buffer-containing tubes maintaining a tissue-to-buffer ratio between 1:5 and 1:10 (v/v). Specimen containers require continuous temperature control at 2°C–8°C (eg, ice-packed containers) and must commence immediately on laboratory arrival within 2–4 hours post-collection, with the entire procedure completed within 48 hours.[23 24]
2. Aseptic workflow implementation: All organoid culture consumables (eg, pipette tips, culture plates) must be certified sterile and RNase-free. Liquid reagents lacking pre-sterilisation should undergo filtration through 0.22 µm membranes. All manipulation steps should be conducted under class II biological safety cabinets within ISO 5-certified cleanrooms.[25]
3. Quality control metrics prior to organoid culture: Three key parameters require verification to optimise culture success: Microscopically confirmed tumour cell clusters with intact membranes and minimal apoptosis; Tissue viability: absence of necrosis/purulent exudate; Contamination-free status: no adherent debris or suspended pollutants.

Recommendation 1

Successful generation of patient-derived ECOs necessitates stringent preanalytical protocols: Viable tumour specimens must exceed 5 mm^3 in volume to ensure adequate tumour cellularity, with smaller biopsies prioritised for clinical diagnostics. Precise sampling should target tumour-rich regions while avoiding necrosis and normal tissue contamination. All procedures require aseptic execution in disinfected environments to minimise microbial exposure. Tissues must undergo continuous cold-chain maintenance (2°C–8°C) during transport, with processing initiation within 2–4 hours post-resection, with the entire procedure completed within 48 hours.

Organoid construction and culture protocols

Successful organoid generation requires standardised operational workflows:

Preprocessing preparation

This process involves preoperation calibration of equipment, sterilisation of consumables and prepreparation of reagents under aseptic conditions.

Tissue dissociation

Initial tumour tissue samples must be reserved for histopathological and molecular characterisation. For surgical specimens, effective dissociation requires aseptic mechanical mincing followed by enzymatic digestion (using pathologically tailored concentrations of collagenase, dispase, trypsin or ethylenediaminetetraacetic acid (EDTA), individually or in combination) under temperature- and duration-optimised conditions. Digestion intervals necessitate mechanical trituration every 5–10 min

to synergistically disintegrate tissue aggregates until complete single-cell liberation. Commercial dissociation kits represent validated alternatives.

Cell collection

Postdissociation cells or cell aggregates require thorough washing and filtration to remove residual cellular debris, dissociation reagents, red blood cells and extracellular matrix (ECM). To ensure cellular viability and prevent cell loss, multiple rounds of dissociation and collection may be performed to maximise viability while achieving the highest possible recovery rate.

Cell counting

Viability assessment of dissociated cells should use trypan blue exclusion or Calcein-AM/PI (Acetoxymethyl ester/Propidium Iodide) fluorescence staining to quantify viable cell proportions. The postdigestion cell yield must exceed 10^4 cells with viability ≥90%0.[23]

Culture system

Organoids are embedded in ECM substitutes (Matrigel, Geltrex) or maintained in serum-free, low-adhesion suspension. For expansion, cultures are incubated under hypoxic conditions (5% O_2, 5% CO_2, 37°C) using defined media (eg, DMEM/F12 (Dulbecco's Modified Eagle Medium/Ham's F-12) supplemented with B27, N2, EGF (50 ng/mL), Noggin (100 ng/mL), R-spondin1 (500 ng/mL)).[26] Molecular subtype-specific adjustments (growth factor concentrations, Wnt agonists) are empirically determined.[26]

Quality control

Successful establishment of ECOs must satisfy three criteria: Primary cultures must develop organoids exceeding 50 µm in diameter within 1–2 weeks; Quantified metabolic activity (via Cell Counting Kit-8 (CCK-8)/Alamar Blue assays measuring cellular reductase activity) on day 6 postpassaging must be significantly higher than on day 3; Continuous expansion ≥3 passages with maintained morphological consistency postpassaging and postcryorecovery. Systematic studies on ECOs success rates across molecular classification remain limited. Current data from a doctoral dissertation indicate establishment rate of 81.3% for *POLE*-mutated (POLEmut), 86.8% for mismatch repair deficiency (MMRd), 64.5% for p53abn (P53 abnormal), and 86.5% for no specific molecular profile (NSMP) subtypes.[27]

Organoids passaging

ECOs require passaging when reaching diameters of 100–200 µm (typically after 1–2 weeks per passage), as unchecked growth induces central necrosis in solid organoid cores due to diffusion limitations. The passaging process entails enzymatic dissociation and washing procedures, during which cellular loss must be minimised while maximising postprocedure viability.

Cryopreservation and recovery

For biobanking, organoids are resuspended in serum-free cryomedium, subjected to controlled-rate freezing and stored at −80°C (short-term) or liquid nitrogen (long-term). Thawing employs 37°C prewarmed media (5–10×dilution) with immediate viability assessment.

Organoid validation

During ECOs culture, comparative assessments must be conducted between organoids and source tumour tissues, evaluating consistency in morphological characteristics, cancer marker profiles and genetic mutation features to validate model fidelity.

1. Morphological consistency

H&E staining confirms that organoids recapitulate key tumour characteristics of EC including nuclear hyperchromasia and pleomorphic epithelial architecture,[13] with mandatory review by a certified pathologist.

2. Histopathological morphology

Immunohistochemistry (IHC) analysis of ECOs confirms biomarker expression concordance with source tumours. Per WHO 2020 endometrial cancer classification guidelines, histomorphology underpins classification and clinical management, supplemented by IHC in complex cases.[22] Core biomarkers include: oestrogen receptor, progesterone receptor, proliferation indices (Ki-67), MMR proteins (MLH1, MSH2, MSH6, PMS2), oncogenic drivers (p53, PTEN, β-catenin), aberrant patterns (MMRd: ≥1 MMR protein loss; p53abn: mutant-p53 overexpression) must mirror parental tumour profiles.[28]

3. Genomic mutations and molecular validation

Genomic profiling during organoid establishment confirms concordance with primary tumours. Standard endometrial cancer biomarkers comprise: Driver genes: PTEN, PIK3R1, PIK3CA, FBXW7, KRAS; MMR genes: MLH1, MSH2, MSH6, PMS2, EPCAM; Chromatin remodelers: ARID1A, ARID1B, ARID5B, RPL22, CTCF, SMARCA4 (BRG1), SMARCB1 (INI1); Other: CTNNB1, PPP2R1A, SPOP; Microsatellite status: BAT25, BAT26, D5S346, D2S123, D17S250 (MSI-H: ≥2 unstable loci). Organoid validation requires stepwise comparison of POLE status, MSI/MMR mutations and TP53 variants against parental tumour molecular subtyping.

At present, there are no established standards or thresholds for evaluating mutational consistency between organoids and primary tumours. In a study by Zhao *et al*, comparison of 15 bladder cancer organoids with matched primary tumours revealed a copy number similarity >50% and a shared single nucleotide variant ratio of 74.7% (±18.0%).[29] In research by Hans Clevers, tumours and organoids from three SCCOHT (small cell carcinoma of the ovary, hypercalcemic type) patients consistently carried both germline and somatic mutations in the SMARCA4 gene, including missense, nonsense and frameshift mutations.[30] The concordance rate of microsatellite status between the organoids with whole exome sequencing and the parental tissues in our team

is 93.33%, and the concordance rate of molecular typing is 86.67%.[27]

4. Tumour heterogeneity features

Single-cell RNA sequencing (scRNA-seq) enables high-precision cellular-level analysis of cell composition, classification, gene expression and heterogeneity within tumours and across pathological subtypes, while spatial transcriptomics delineates in situ spatial topological features of the tumour microenvironment. This validation must be integrated during organoid establishment processes.

A summary of the fidelity validation for ECOs is provided in table 1.

Recommendation 2

The establishment of reproducible and clinically relevant ECOs requires the implementation of standardised operating procedures covering tissue dissociation, cell isolation, culture expansion, cryopreservation and validation. ECOs establishment should meet three criteria: (1) primary organoids exceeding 50 µm in diameter within 1–2 weeks; (2) significantly elevated metabolic activity between day 3 and day 6 after passaging and (3) sustained expansion over at least three passages while maintaining morphological stability post-passaging and post-thaw. Organoids should be passaged at 100–200 µm (typically every 1–2 weeks). Organoid validation constitutes a critical step requiring integrative assessment of histopathological features, biomarker profiles and genomic alterations to ensure biological fidelity. ECOs should demonstrate identical molecular subtypes to primary tumours.

Establishment and management of ecos biobanks

The expanding scale and data throughput of biobanking necessitate integrated organoid biobanks to systematically catalogue, retrieve and visualise experimental data. Such infrastructure maximises research impact by enabling data sharing and deep mining, ultimately advancing disease prevention/therapeutics. Diverse tumour-specific organoid biobanks have been established,[31–35] with their construction offering two strategic advantages: prospective utility, leveraging pharmacogenomic big data to predict drug responses from patient expression profiles, while integrating clinical metadata, experimental validation and multiomics datasets to elucidate novel biological mechanisms; retrospective value, ensuring data integrity through auditable experimental trails and facilitating knowledge consolidation/sharing via structured repositories.

Ethical approval and patient informed consent

The establishment of ECOs Biobanks requires compliance with rigorous ethical review procedures, acquisition of informed patient consent, and protection of patient data and biological sample security.

Organoid biobanks require integrated infrastructure encompassing

(1) Core functional zones: aseptic processing areas with class II biosafety cabinets, climate-controlled culture zones using stable CO_2 incubators (±0.1°C), and ultra-low temperature storage featuring vapour-phase liquid nitrogen tanks/−80°C freezers with multipoint monitoring; (2) Key equipment: controlled-rate freezers, phase-contrast inverted microscopes, automated liquid

Table 1 Validation criteria for endometrial cancer organoids

Validation category	Test item and methodology	Mandatory/ recommended
Bright-field morphology	Endometrial cancer organoids exhibit hollow spheroid or spheroid-like architectures under phase-contrast microscopy, characterised by a tightly packed outer cellular layer with high density and a translucent core. Subtypes include solid, cystic or irregular morphologies, with some specimens showing coexisting hollow and solid regions	Mandatory
Histopathological morphology	H&E staining reveals hyperchromatic nuclei, nuclear atypia and mitotic figures within organoid structures	Mandatory
Pathological features	IHC and immunofluorescence validate concordance of histopathological markers between organoids and matched primary tumours	Mandatory
Genomic mutations and molecular characteristics	WES/targeted sequencing analysis confirms concordance in POLE mutation status (exonuclease domain), MSI/MMR gene alterations, TP53 mutation hotspots and other key gene mutations with parental tumour	Mandatory
Tumour heterogeneity features	scRNA-seq delineates cellular composition heterogeneity, identifying tumour epithelial, stromal and immune subsets. Spatial transcriptomics enables the spatially resolved mapping of gene expression profiles	Recommended

IHC, immunohistochemistry; MMR, mismatch repair; MSI, microsatellite instability; WES, whole exome sequencing.

handlers (recommended), and bulk liquid nitrogen supply systems; (3) robust safeguards: such as dual power grids with backup generators and independent HPLC (High Performance Liquid Chromatography)-grade water/medical-gas systems; (4) QC laboratories equipped with molecular biology (qPCR, flow cytometers) and histology platforms and (5) Management system: Full-process sample tracking and data management.

Construction of the ecos banks

Through analysis of molecular pathological characteristics, genomic sequencing and transcriptomic data of ECOs, the biobank architecture stratifies endometrial carcinoma organoids into four molecular subtypes per WHO/TCGA criteria: *POLEmut*, MMRd, NSMP and p53abn, ensuring diversity across histopathological and molecular spectra.

Quality control of standardised organoid biobanking

Establish standardised protocols to ensure stable viability during cryopreservation, revival and culture processes, minimising sample attrition and genomic/phenotypic variation through rigorous batch-to-batch validation.

Data sharing and collaborative research

Implement a centralised biobank information management system to synchronise clinical metadata, including molecular profiles, demographics, clinical history, pathological annotations, outcome metrics. All data management and sharing activities will be conducted in full compliance with Chinese regulations, particularly those governing human genetic resources. To ensure data utility and collaboration while adhering to these regulations, we recommend adherence to the FAIR Guiding Principles and encourage deposition into nationally recognised or domestically authorised biomedical data repositories.

Recommendation 3

The establishment of ECOs biobanks demands standardised protocols and governance frameworks to ensure ethical and regulatory compliance. Given the substantial human and financial resources required, healthcare institutions may engage in public-private partnerships to facilitate biobank development, provided patient rights and data sovereignty are rigorously protected. Strategic translation of biobank resources into clinically actionable assets—guided by benefit-sharing principles and aligned with international standards—can amplify socioeconomic value while advancing precision oncology innovations.

Translational applications of ECOs

ECOs serve as ideal platforms for drug sensitivity assessment, which recapitulate tumour heterogeneity and molecular signatures while offering in vitro culture tractability. Systematic drug screening using these organoids enables prediction of individualised therapeutic responses, thereby informing personalised treatment strategies. Additionally, these models serve as powerful tools for investigating endometrial carcinogenesis mechanisms, particularly in identifying key oncogenic pathways and driver gene alterations. Furthermore, by incorporating stromal, vascular and immune microenvironment components, ECOs can be engineered into 3D self-integrating micro-physiological systems, providing a high-fidelity research model for screening immune checkpoint inhibitors, anti-angiogenic agents and elucidating their mechanistic underpinnings.

Personalised drug sensitivity profiling and high-throughput screening

Organoid-based drug sensitivity testing offers high-throughput screening (HTS) capacity, precise predictive accuracy and rapid reporting timelines. Studies have demonstrated the feasibility of personalised organoid screening models across various treatment stages and modalities, providing clinical benefits for patients.[36 37] The expert consensus of clinical application about tumour precision therapy guided by organoid-based drug sensitivity testing (2022 edition) recommends tumour organoid drug sensitivity testing in clinical scenarios such as standard therapy failure, rare or refractory malignancies lacking established regimens, low-evidence guideline recommendations, multiple primary tumours requiring therapeutic prioritisation, and off-label drug applications.[38] Notably, Vlachogiannis *et al* reported that colorectal cancer organoid testing achieved 93% specificity, 100% sensitivity, 88% positive predictive value and 100% negative predictive value.[39] Recent meta-analyses further indicate that organoid platforms attain 84% overall sensitivity and 81% specificity in predicting treatment responses across gastrointestinal malignancies, including oesophageal, gastric, pancreatic and colorectal cancers.[40]

Screening platform

HTS platforms use automated equipment and microplate technology to rapidly screen large compound libraries. Common HTS devices include automated liquid handlers, microplate readers and imaging systems. Microplates are typically 96-well or 384-well formats, with plate specifications selected based on experimental needs. Manual screening approaches are also feasible.

Organoid seeding

Endometrial carcinoma organoids are cultured to an optimal size (typically 50–200 µm in diameter) and dissociated into single-cell suspensions or small clusters via mechanical or enzymatic digestion. The cell suspension is homogenously resuspended in Matrigel (medium : Matrigel ratio=2:8) and seeded into microplates at 500–2000 cells/well (96-well plate), followed by incubation at 37°C with 5% CO_2 to re-establish organoid structures. Inter-well consistency is assessed using the coefficient of variation (CV), with CV <15% indicating reliable reproducibility.

Drug administration

After organoid stabilisation, automated or multichannel pipettes are used to add drug solutions at varying concentrations to the microplates. Dose-response relationships are evaluated via serial drug dilutions, with each concentration tested in ≥3 replicate wells to ensure data

robustness. This protocol excludes immune checkpoint inhibitors and anti-angiogenic agents.

Viability assessment and data analysis

Drug sensitivity is quantified using methods such as the CCK-8, ATP-based fluorescence endpoint assays, or real-time metabolic fluorescence detection. Absorbance/fluorescence data are exported, normalised and cleansed of outliers to ensure consistency. Preliminary analysis and visualisation are performed using software such as Excel or GraphPad Prism. Inhibition rates are calculated for each drug concentration, and dose-response curves are generated.

Recommendation 4

Organoid drug screening may guide treatment for advanced/recurrent endometrial carcinoma when standard options are exhausted, provided ethical approval and informed consent are secured (see supporting evidence above).[36–40] Clinical integration requires prospective validation of predictive accuracy, incorporating toxicity assessments.

Investigating endometrial carcinogenesis and key signalling pathways

ECOs preserve tumour heterogeneity and microenvironmental complexity, serving as powerful tools for studying carcinogenesis and critical signalling pathways. Boj *et al* demonstrated the utility of organoids in pancreatic cancer by integrating gene expression and proteomic analyses of normal, precancerous and malignant organoids, identifying progression-associated molecular pathways.[41] Similarly, Sengal *et al* applied FGFR inhibitors in endometrial carcinoma organoids, revealing the pivotal role of FGFR2c signalling in tumourigenesis and validating it as a therapeutic target.[42] CRISPR-based gene editing enables the creation of single-gene or multigene mutation models to dissect functional impacts on proliferation, differentiation and metabolism. Our prior work identified MYC overexpression as a dominant driver of endometrial malignant transformation through functional scoring of oncogenic potency in CRISPR-edited normal endometrial organoids.[20]

Tumour microenvironment modelling

Co-culture systems integrating stromal, immune or vascular cells with tumour organoids recapitulate cell-cell interactions within complex microenvironments.[43 44] For instance, refined fibroblast-lung cancer co-culture models mimic fibroblast-induced phenotypic shifts and enhanced metastatic potential.[45] Organoid-on-chip (OOC) technology further enhances physiological relevance by embedding mature organoids into microfluidic devices that simulate dynamic nutrient exchange, waste removal and biomechanical cues.[46] Vascularised OOCs, incorporating 3D-bioprinted capillary networks, overcome hypoxia-induced necrosis in large organoids (>400 µm), enabling long-term culture of physiomimetic tissues.[47–49] These platforms have been preliminarily applied in lung, breast and colorectal cancers.[50–53] Hans Clevers' recent study established a PDO-PBMC (Peripheral Blood Mononuclear Cell) co-culture model by encapsulating both intestinal organoids and immune cells within a solid 3D hydrogel which provides a powerful tool for improving the preclinical assessment of cancer immunotherapies.[54] Similarly, Ren *et al* created 3D T - cell - incorporated cervical squamous cell carcinoma (CSCC) organoid models to mimic the interaction between CSCC and T cells.[55]

Interdisciplinary integration and advanced technologies

Integrating organoid drug screening data with clinical patient profiles through bioinformatics and artificial intelligence enables the development of precision prediction models, significantly enhancing the accuracy of personalised therapeutic forecasts.[56 57] Beyond HTS, organoids demonstrate considerable potential in pharmacogenomics—by correlating genomic sequencing data with drug sensitivity profiles, they elucidate mechanistic relationships between genetic mutations/expression patterns and therapeutic responses, thereby providing a scientific foundation for precision oncology strategies.

Recommendation 5

ECOs are validated preclinical models for investigating disease pathogenesis, developing molecular targets and evaluating therapeutic candidates. Establishing immune-competent ECOs and vascularised ECOs platforms is essential to overcome functional limitations associated with tumour microenvironment absence.

Future perspectives

Endometrial carcinoma organoids hold transformative potential for elucidating carcinogenic mechanisms, identifying therapeutic targets, guiding personalised therapies and advancing preclinical drug development. However, large-scale clinical trials leveraging PDOs remain scarce, with limited datasets on biobanking and clinical translation. Current challenges necessitate interdisciplinary convergence, particularly in addressing vascularisation and architectural maturation through bioengineering innovations such as microfluidic systems and biomaterial scaffolds. Standardisation efforts must integrate emerging technologies—including 3D bioprinting, artificial intelligence-driven quality control and real-time biosensing—to achieve scalable and reproducible organoid models. Furthermore, immune-competent co-culture systems and vascularised organoids are critical to recapitulating the complexity of tumour microenvironments and improving drug response predictability.

This consensus presents China's inaugural English-language expert consensus on standardised methodologies and clinical translation initiatives for ECOs. As an evolving framework, it will undergo iterative refinement informed by emerging global evidence, ultimately establishing precision guidelines. Research on vascularised organoids and the establishment of immune cell co-culture systems is currently underway, aiming to develop models that more closely resemble the complex in vivo tumour microenvironment and better reflect the characteristics of original tissues and their responses to therapeutics. Current limitations in drug metabolism/toxicity profiling necessitate complementary

models (eg, multiorgan chips, animal models) for comprehensive assessment.

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