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Review Article

Organoid technology in cervical cancer research

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Abstract: Cervical cancer poses a serious threat to women's lives and health, and it may cause damage to the reproductive system, infertility, and even death. This study reviews the research progress of organoids in the treatment of cervical cancer. Studies have found that the culturing of tumor cell lines and the modeling techniques of tumor xenotransplantation for cervical cancer have certain limitations. Cervical cancer organoids are preclinical research models formed by culturing tumor cells derived from patients, which more accurately and effectively retain tumor heterogeneity, and also have the potential to take into account the interaction between tumor cells and the extracellular matrix. This article reviews the research on cervical cancer organoid models in the pathogenesis, drug screening, and precision medicine aspects in recent years, and then analyzes the development prospects and challenges of organoid technology in gynecological tumor research, in order to explore new possibilities for individualized treatment of cervical cancer.

Keywords: Organoid, cervical cancer, precision medicine, drug screening experiments, preclinical model

Introduction

According to the definition of the World Health Organization (WHO), those over 65 years old are classified as the elderly [1]. Data from China's seventh national census shows that in 2021, there were 190 million elderly people over 65 years old, accounting for 13.5% of the total population, and it is expected that the proportion will reach 28.7% in 2050. The aging process is unstoppable [2, 3]. The 2021 World Health Organization Statistical Report shows that the average life expectancy of Chinese women is 80.5 years old [4-6]. The latest data from ICO/IARC China shows that in 2020, the number of new cases of cervical cancer in elderly women over 65 years old reached 17,886, and the number of deaths reached 18,110, with a higher proportion in rural areas than in cities; as of December 31, 2016, among women over 60 years old, those who had ever undergone cervical cancer screening accounted for only 10.8% of this group [7-11]. Due to various factors, the screening rate of cervical cancer in elderly Chinese women is low, which has led to cervical cancer, which could have been prevented and treated, becoming one of the main risk factors threatening their health and life [9, 12].

Cervical cancer is a malignant tumor of the female reproductive system that occurs in the cervix and ranks second in the incidence of female malignancies in China [4, 13]. In recent years, with the popularization of early screening for cervical cancer and HPV vaccines, cervical cancer can be detected, diagnosed, and treated early. Its incidence has shown a gradual downward trend [10, 12]. However, there are still limited precise treatment methods for advanced or recurrent cervical cancer [14, 15]. How to propose individualized treatment strategies based on its unique marker proteins or genes is a challenge faced in improving the prognosis of patients with cervical cancer [16-21].

With the development of oncology and stem cell biology research based on organoid culture

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technology, its construction technology is also constantly improving, and organoid technology has been proved to be a good in vitro culture model of human organs and tissues [22-25]. Organoid technology has been extended to the research of various gynecological tissues and tumors, including normal fallopian tubes, ovarian surface epithelium, endometrium, and related cancers [26]. This article summarizes and elaborates on the progress in the culture of cervical cancer organoids and their application and challenges in tumor research in recent years, to provide a reference for the application of organoid technology in gynecological tumor research [27].

Overview of organoids

Organoids can be developed by differentiating and culturing embryonic stem cells, adult stem cells, or induced pluripotent stem cells in a three-dimensional manner [28]. In an in vitro environment, by adding Matrigel and various cytokines, stem cells self-assemble similarly to that in vivo [29]. Organoids can highly simulate the physiological structure, function, development, and differentiation process of the in situ tissue. They can be widely used in research fields such as drug development, disease modeling, cancer research, developmental biology, regenerative mechanisms, precision medicine, and organ transplantation [30, 31].

The growth of organoids primarily relies on the support of various cytokines and the three-dimensional environment provided by Matrigel [32]. These cytokines mainly include activators, inhibitors, and hormones that promote cell growth and differentiation-related pathways; cytokines that promote cell proliferation; and cytokines added to enhance the success rate of organoid culture, etc. [33]. By adding Wnt pathway agonists R-spondin, transforming growth factor-β (TGF-β) inhibitor Noggin, EGF, etc. to the basal medium, small intestinal organoid structures with crypts and villi have been successfully cultivated [32, 34]. This culture protocol has laid a solid foundation for developing organoid technology [35]. Based on this, the laboratory further added nicotinamide, anaplastic lymphoma kinase (ALK) inhibitor A-8301, prostaglandin E2 (PGE2), and p38 inhibitor SB202190, etc. to the improved formula, successfully establishing a human colorectal tumor organoid system [36]. On this basis, various laboratories have successively developed organoid systems of multiple tissues by adding or subtracting different cytokines [37]. In constructing the three-dimensional system, extracellular matrix gel was commonly used as a three-dimensional scaffold in the early stage [38]. However, the culture of Matrigel may inhibit the growth and maturation of organoids by restricting the exchange of gases and metabolites between organoids and the surrounding microenvironment [33]. Therefore, Matrigel has gradually been replaced by sponge-like or fibrillar scaffolds containing larger cavities [39]. Using the internal vascular network of the liver as a scaffold better promotes the transportation of nutrients in organoids and significantly improves the in vitro survival rate of organoids [40]. These breakthrough novel scaffolds have significantly advanced the continuous development of organoid technology.

To better preserve the heterogeneity of patients, the human tumor and immune microenvironment, various organoid culture systems have been established successively, from the most basic organoid embedding or droplet method, to the derivation of the air-liquid interface method, co-culture method, etc. [41, 42]. In recent years, several studies have successfully constructed tumor immune organoid systems through the holistic method or the reductionist method [43]. A gas-liquid planar organoid model containing epithelial and stromal compartments and specific tumor-infiltrating lymphocytes was reported through the holistic method [44]. In addition to the basal medium, additional T cell activators, such as interleukin-2 (IL-2), were added to support the growth of immune cells [45]. Therefore, multiple types of immune cells, such as CD8+ T cells, CD4+ T cells, B cells, natural killer (NK) cells, and natural killer T (NKT) cells, can survive for several days in this system [46]. In the reductionist system, organoids can be taken from patient surgical specimens or biopsy specimens and co-cultured with immune cells from the peripheral blood of the same patient to achieve long-term co-culture (**Figure 1**) [47]. Therefore, the various systems developed based on the organoid system can meet the different growth and expansion needs of organoids and provide a good research platform for tumor microenvi-

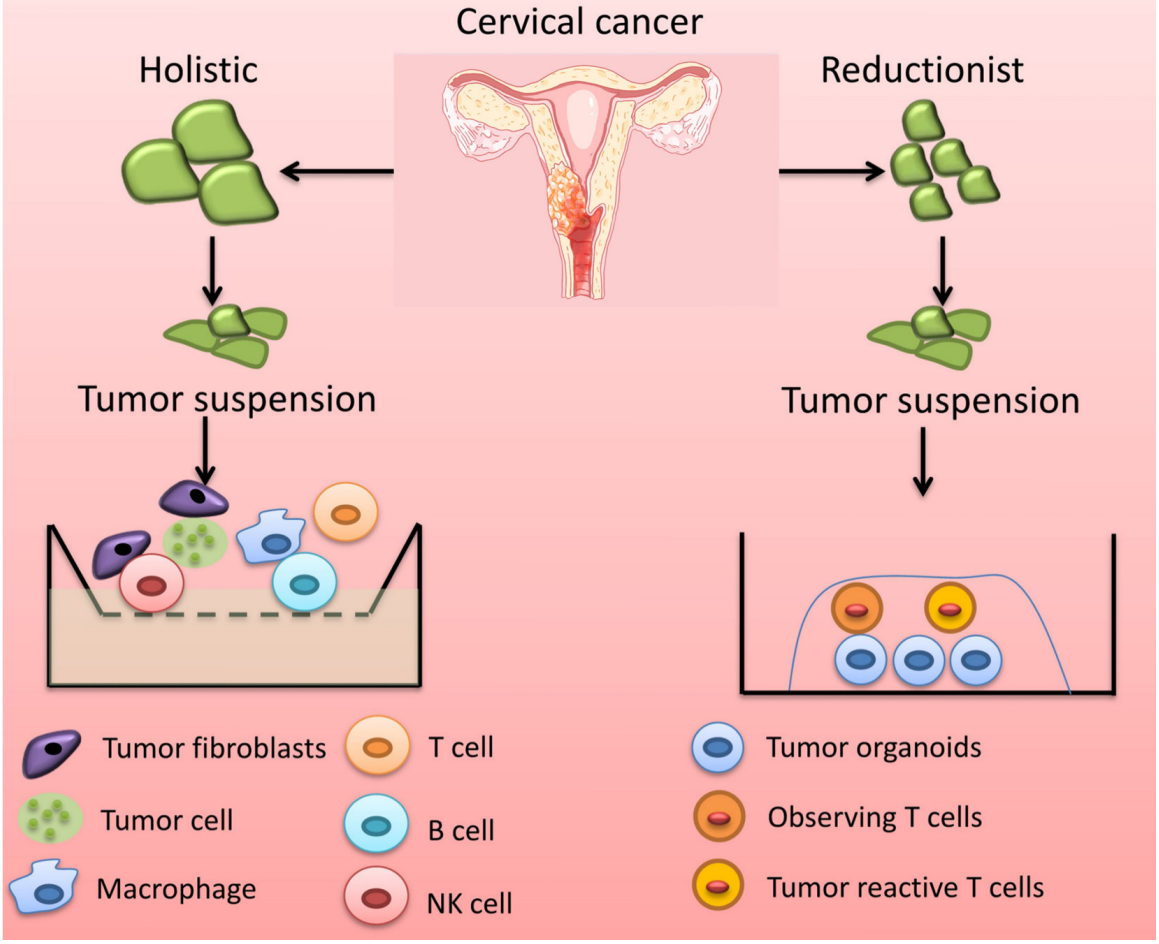

Figure 1. Application of holistic and reductionist approaches in cervical cancer research. This figure illustrates the different applications of holistic and reductionist approaches in cervical cancer research. The holistic approach focuses on the multicellular interactions within tumor tissue, including tumor fibroblasts, tumor cells, macrophages, T cells, B cells, and NK cells, to better mimic the in vivo microenvironment. The reductionist approach, on the other hand, utilizes tumor organoid cultures and specific immune cells (such as observing T cells and tumor-reactive T cells) to study immune responses in cervical cancer.

ronment research and individualized treatment of tumor immunity.

Development of organoid technology

Organoids not only retain histological and genetic features highly similar to those of in vivo organs, but also have extremely high clinical relevance in predicting anti-cancer drugs [48, 49]. They have been widely used in basic tumor research and clinical transformation, including tumor organoid sample banks, the construction of tumor microenvironments, the study of tumorigenesis and development mechanisms, and personalized drug screening, as shown in **Figure 2** [50, 51].

Construction of tumor like organs

Tumor organoids are 3D primary tumor cell cultures that retain the histological and mutational characteristics of the original tumor [52]. Patient-derived tumor organoids [PDOs] can generally be constructed by biopsy and surgical resection of the tumor, and the tumor cells are encapsulated in the extracellular matrix (ECM) and require the addition of specific growth factors in the growth medium for culture [53]. The culture methods of PDOs vary depending on the type of tumor [54]. Currently, most tumor organoids are cultured using Matrigel hydrogels, which are a mixture of colloidal proteins secreted by mouse sarcoma cells [55]. The

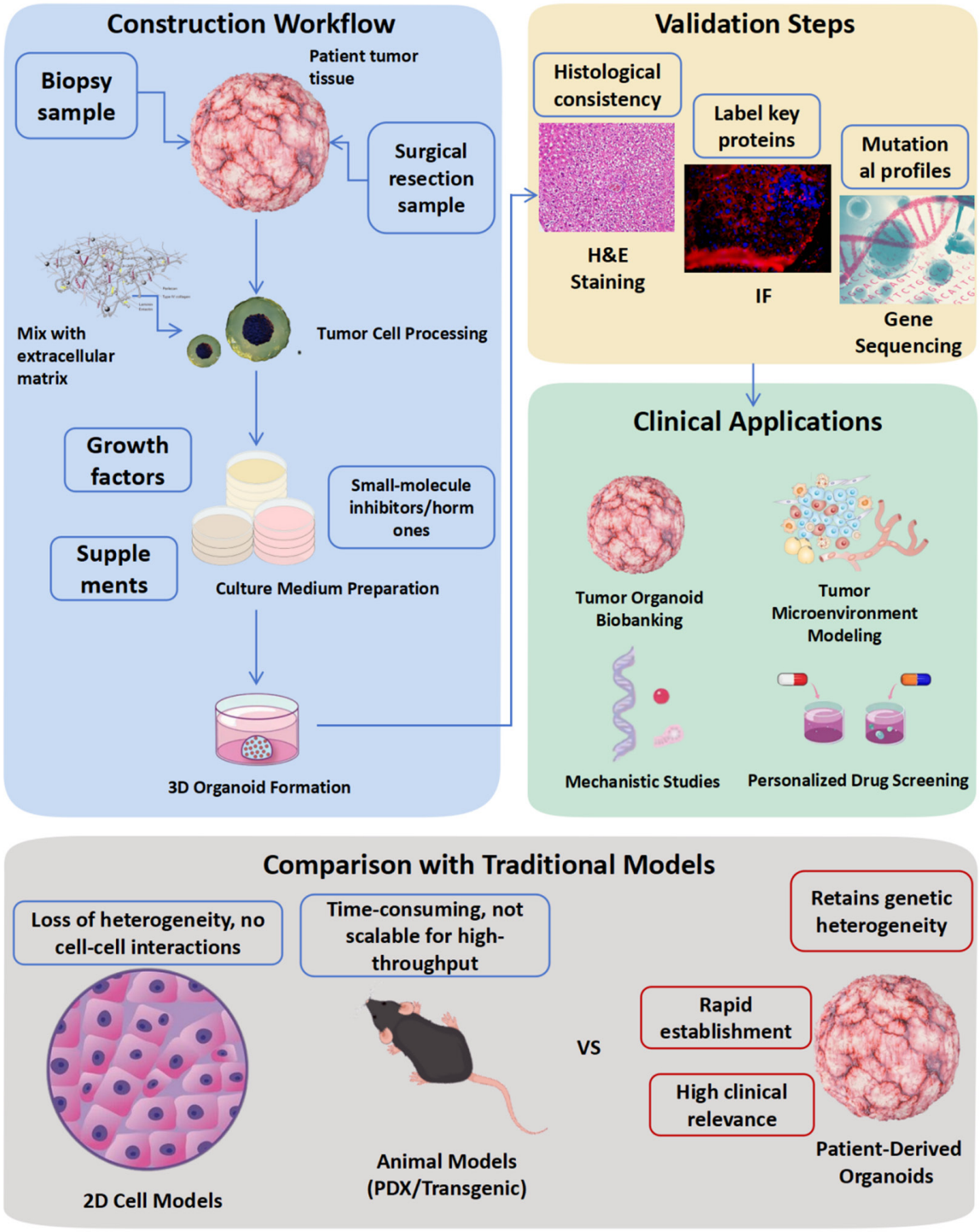

Figure 2. Workflow and clinical applications of patient-derived tumor organoids (PDOs). This figure outlines the construction, validation, and clinical utilization of PDOs. Tumor tissues from biopsies or surgeries are processed into 3D organoids using Matrigel and growth factor-enriched culture systems. Validated through histology (H&E), protein markers (immunofluorescence), and genetic profiling, PDOs retain the original tumor's characteristics. They are further applied to biobanking, tumor microenvironment studies, mechanistic exploration, and personalized drug testing. Comparisons highlight PDO advantages (genetic fidelity, rapid generation) over traditional 2D cultures (heterogeneity loss) and animal models (time-consuming limitations), emphasizing their role in accelerating cancer research and precision therapy.

Table 1. The characteristics of 2D cell lines, PDX, and PDOs in modeling and drug screening of cervical cancer

Group	2D cell line	PDX	PDOs
Tumor modeling			
Time	Longer	Long	Shorter
Source of microenvironment	No	Mice	Co-cultivation
Tumor heterogeneity	Homogeneity	Heterogeneity	Heterogeneity
Tumor stage	Advanced	Advanced	Early to late stages
Drug screening			
Cost	Low	High	Higher
Time	Short	Long	Longer
High throughput drug screening	Fast	Unable to achieve	Faster
Clinical response correlation	Weak	Strong	Strong

Note: This table summarizes the characteristics of different experimental models used for cervical cancer research, including 2D cell lines, patient-derived xenografts (PDX), and patient-derived organoids (PDOs). It compares their suitability for tumor modeling and drug screening based on factors such as time, microenvironmental relevance, tumor heterogeneity, cost, and clinical correlation.

composition of the medium depends on the type of organoid model, including various growth factors [R-spondin, Wnt3A, fibroblast growth factor, epidermal growth factor, Noggin, etc.], HEPES, GlutaMAX, nicotinamide, B27, small molecule inhibitors, and various hormones that promote the growth of organoids [56]. The success of organoid construction must be verified and evaluated through multiple dimensions such as HE staining, immunofluorescence, and gene sequencing; confirming the consistency between the organoid and the original tumor is a prerequisite for subsequent studies [57, 58].

The advantages of tumor like organs

In cancer research, traditional 2D cell cultures and animal models have played essential roles in basic research, but both models have certain limitations [59]. 2D cell cultures require a significant amount of time to establish continuous passages of tumor cells, making it difficult to maintain the expression of key driver genes in various cell subtypes and the parental tumor [60]. Cell lines, as in vitro selected products, inevitably lead to the loss of tumor molecular characteristics during the selection process, including copy number variations, mutations, and internal heterogeneity [61-63]. Moreover, monolayer cultures of cells cannot simulate the interaction between cells in vivo, which is crucial for regulating signal pathways and gene expression and is the basis for cells to exert biological functions [64].

Commonly used animal models include transgenic models and PDX [65]. Animal models generated through genetic engineering cannot truly simulate the pathogenic process in humans, and the generation of this model is also very time-consuming [66]. In contrast, PDX models, which are constructed by directly transplanting part of the freshly resected patient's tumor into the animal model, can better preserve the important characteristics of the tumor [67]. However, PDX models require a relatively long time to construct to have high transplantation efficiency and show host infiltration characteristics of tumor cells [68]. The derivation efficiency of cell lines and PDX is low, and they cannot contribute to large-scale individualized treatment. In addition, these two models usually come from advanced tumors, so they cannot fully capture the physiological characteristics of the entire cancer development process. PDOs are constructed from tumors within the first few weeks after surgical resection, and their greatest advantage is that they can effectively retain the genetic and phenotypic heterogeneity of patients [69]. Compared to 2D culture cell lines using serum-containing medium, primary tumor organoid cells accumulate fewer genetic variations during multiple passages [70]. The characteristics of the three models in tumor modeling and drug screening are shown in **Table 1**.

Progress in organoid culture of cervical cancer

Recent advancements in cervical cancer organoid culture have focused on optimizing proto-

cols to better replicate tumor heterogeneity and microenvironmental interactions. Key progress can be categorized into three areas:

Culture protocol standardization

The matrix bilayer organoid culture (MBOC) system, utilizing Matrigel as a scaffold to mimic the cervical extracellular matrix, has emerged as a foundational method for establishing cervical cancer organoids [71]. This protocol supports long-term culture by incorporating critical cytokines and growth factors. Notably, studies highlight the necessity of modulating the Wnt/β-catenin signaling pathway - specifically through ligands like RSPONDIN-1 and Wnt3a - to maintain stemness and drive self-renewal in cervical squamous cell carcinoma organoids [72, 73]. Further refinement of culture conditions, such as adjusting oxygen levels and nutrient gradients, has improved organoid viability and phenotypic stability [74].

Pathological subtype-specific modeling

Cervical cancer organoids now successfully model major histological subtypes. Squamous cell carcinoma [SCC] organoids, representing 70% of cases, exhibit dense cellular structures but face lower culture success rates compared to adenocarcinoma organoids [25% incidence], which form cystic architectures [75, 76]. This divergence underscores the influence of pathological origin on organoid morphogenesis. Recent breakthroughs include the establishment of rare subtypes, such as clear cell carcinoma and small cell neuroendocrine carcinoma organoids [77]. These models address a critical gap in studying malignancies lacking clinical trial data, enabling personalized drug testing [78].

Genetic and microenvironmental recapitulation

Transcriptomic analyses confirm that cervical cancer organoids retain HPV-driven genomic signatures and tumor-specific gene expression profiles, closely mirroring parental tissues [79]. CRISPR-Cas9 editing has further enabled the generation of genetically defined organoids, such as HPV oncogene knockout models, to dissect viral carcinogenesis [80]. Additionally, co-culture systems integrating stromal cells or immune components are being explored to replicate tumor-immune interactions, overcoming limitations of traditional PDX models [81].

These advances highlight the potential of organoids to serve as high-fidelity platforms for studying cervical cancer biology and therapeutic responses. However, challenges persist in standardizing culture success rates across subtypes and scaling production for clinical applications. Matrigel can form and maintain cultures.

Application of organoids in the pathogenesis of cervical cancer

Organoid models have emerged as powerful tools to dissect the molecular mechanisms underlying cervical carcinogenesis, particularly in HPV-driven tumorigenesis and host genetic alterations. Key applications include:

Modeling HPV-driven oncogenesis

High-risk HPV infection initiates a multi-stage carcinogenic process, primarily mediated by viral oncoproteins E6 and E7, which inactivate tumor suppressors p53 and pRB [82, 83]. Organoids recapitulate HPV-DNA integration events and their downstream genomic consequences, such as oncogene amplification and chromosomal rearrangements [84]. For example, HPV18-transfected cervical transformation zone organoids revealed that HPV integration triggers transcriptional dysregulation of NPM3, a novel therapeutic target in cervical adenocarcinoma [85]. Additionally, co-culture models combining HPV and Chlamydia trachomatis-infected cervical organoids demonstrated synergistic activation of inflammatory pathways [e.g., NF-κB], accelerating epithelial-mesenchymal transition (EMT) and cellular reprogramming [86]. Single-cell transcriptomic analysis of HPV16-infected organoids further identified precancerous keratinocyte subpopulations with distinct gene expression profiles, providing spatial insights into early malignant transformation [87].

Host genetic and genomic heterogeneity

Cervical cancer organoids retain tumor-specific genomic alterations, including somatic mutations (e.g., PIK3CA, FBXW7, KRAS) and copy number variations identified by TCGA [88, 89]. These models preserve intratumoral heteroge-

neity and biallelic TP53 inactivation, mirroring the genetic landscape of parental tumors [75, 90]. For instance, Seol et al. [91] established organoids from four cervical cancer subtypes, confirming retention of somatic mutations and clonal diversity. Maru et al. [92] generated organoids from rare clear cell carcinomas, which faithfully reproduced histological features and HPV integration patterns, enabling mechanistic studies of under-researched subtypes.

Disease progression and microenvironment interactions

Organoids have been instrumental in modeling the continuum from precancerous lesions to invasive carcinoma. Hu et al. [27] developed a novel organoid system simulating HPV-associated cervical intraepithelial neoplasia (CIN) and squamous cell carcinoma, capturing transcriptional shifts during malignant progression. These models revealed upregulated tissue-specific genes (e.g., MMP-7, AGR2) in transformation zone organoids compared to traditional cell lines, highlighting their superiority in mimicking in vivo gene expression dynamics [93, 94]. Furthermore, Kusakabe et al. [95] established HPV18-positive small cell neuroendocrine carcinoma organoids, demonstrating KRAS pathway dependency and validating targeted therapy responses.

Cervical cancer organoids in precision medicine

Cervical cancer organoids can display the phenotypic characteristics of cervical cancer in vivo and in vitro, providing a valuable model for the molecular study of patient-specific drug responses, thereby determining the optimal dose of tumor drugs while reducing damage to normal tissues [96, 97]. Studies have reported that the cycle from extracting cancer cells to forming organoids and obtaining clear data is 3 weeks, and using a high-throughput system can achieve drug screening using organoids within 1 week after surgery [18, 98]. Four types of organoids from different cervical cancers were established, and their sensitivity and resistance to the first-line chemotherapy regimens for cervical cancer were tested, indicating that organoids can be used in various screening tests for cervical cancer chemotherapy drugs [91]. The team also conducted high-throughput drug screening from 171 molecularly targeted compounds and obtained 7 compounds that could significantly inhibit the viability of cervical cancer organoids [26]. These results suggest that organoid models can be used to evaluate the patient's response to drugs and predict the drug resistance of the target drug [99, 100]. Using drug sensitivity tests on cervical cancer patient-derived organoids, it was revealed that the beta-blocker propranolol can enhance the therapeutic effect of the oncogene transcriptional inhibitor trabectedin in treating cervical cancer [101]. A HPV18-related cervical small cell carcinoma organoid was established, and new therapeutic targets were identified using transcriptomics and genomics, verifying the inhibitory effects of the KRAS pathway inhibitor trametinib and the proto-oncogene MYC inhibitor MYCi975 on cervical small cell carcinoma organoids [102]. In addition, the organoids were implanted into immunodeficient mice, demonstrating the therapeutic effect of the above anti-cancer drugs on cervical small cell carcinoma, and also showing that the organoids can still maintain the stability of the tissue structure and gene expression profile of the original tumor after xenotransplantation [103]. Therefore, establishing a clinically relevant organoid model can be efficiently used for the sensitivity test of the first-line treatment regimen and restore the complex heterogeneity of individual patients, promoting the development of personalized treatment decisions for cervical cancer [98].

Radiotherapy is one of the main treatment methods for cervical cancer, and the radiosensitivity of cervical cancer patients varies [104]. Determining the radiosensitivity of organoids provides new possibilities for predicting the radiotherapy effect of patients' tumors and exploring the mechanism of radiation resistance [105]. In a prospective study of cervical cancer organoids, it was found that the subtype of cervical cancer with a squamous mesenchymal component as the main tumor had poor sensitivity to radiotherapy [106]. The organoid model proved that the increase of mesenchymal components and the increase of glycolysis level in cancer cells would lead to enhanced radiation resistance of cancer tissues, thereby resulting in poor radiotherapy effect, and it was pointed out that metabolic indicators had certain predictive value for the radiotherapy effect

of cervical cancer [107]. The radiosensitivity of 14 independent cervical cancer organoids to different radiation doses was compared, and the differences in radiosensitivity of cervical cancer organoids from other patients were observed, and the transplantation of organoids into immunodeficient mice was further verified [108]. It is worth mentioning that the team also included tumor-derived organoids from 2 patients with advanced cervical cancer to determine the effect of chemosensitization radiotherapy, and obtained consistent treatment responses with the experimental prediction results in the subsequent clinical follow-up of the patients [109]. These studies all show that at different stages of the development of cervical cancer, in vivo and in vitro sensitivity tests can be carried out with the help of the organoid platform, and help patients achieve precise treatment strategies in a short period [110].

The immune system plays an important role in the process of tumor malignancy [111]. The interaction between HPV-infected cervical cells and the immune microenvironment affects the development of cervical cancer [112]. The primary effector cells of anti-tumor immunity include NK cells and T cells, and the co-culture system of organoids and immune cells provides a new platform for in vitro testing of immunotherapy [113]. An adoptive T cell and cervical cancer organoid co-culture system was established, and the specificity of cervical cancer organoids from different patients for in vitro T cell killing experiments was observed, and it was revealed that TTN gene mutations may be a potential predictor of adoptive T-cell therapy (ACT) for cervical cancer [114]. Studies have also shown that the organoid co-culture system verifies the immunotherapeutic effect of γδT cells on cervical cancer [24, 115, 116]. These all indicate the potential of the organoid platform in predicting the efficacy of immunotherapy in vitro. Due to the complexity and heterogeneity of cervical cancer patients, the efficacy of immunotherapy varies significantly among patients [24]. Therefore, it is necessary to establish a preclinical model of co-culture of immune cells and cervical cancer organoids to accurately evaluate the mechanism and effect of different therapies [95] (**Tables 2**, **3**).

Research dilemmas and challenges

The advantages of organoid models in tumor research are obvious. However, as an emerging technology, its application in gynecological tumors is in its infancy, and there are still areas for improvement and many challenges [117, 118]. Studies have demonstrated that after long-term in vitro culture, organoids derived from tumor tissues contain only malignant epithelial tumor cells, excluding immune cells, blood vessels, or connective tissue [119]. This indicates that organoids lack a true internal environment in the human body, mainly due to the lack of various stromal cells. The absence of these cells can lead to the loss of some internal information of the original tumor, such as organoids derived from malignant epithelial tumor cells being challenging to target drugs that act on the tumor and stroma; for example, tumor vascular endothelial growth factor inhibitors [112]. Some scholars have proposed a way to restore the microenvironment of tumors in the human body by co-culturing organoids with stromal cells and immune cells [26]. By co-culturing NK cells, DC cells with tumor organoids, it was found that the recognition pathway of programmed death receptor 1 and ligand (PD-1/PD-L1) in tumor cells within organoids could be blocked, thereby hindering tumor progression. Our team in China has also conducted in-depth exploration of the specific microenvironment and unique immune response pattern of cervical cancer, forming co-cultured organoids from tumor epithelial cells, endothelial cells, and fibroblasts, and verifying the interaction and function of different cell types in the tumor microenvironment at the molecular level through transcriptomics. There is still a lot of room for exploration on how organoid technology can completely restore the true immune environment in the body and play a greater application value in tumor immunotherapy research [97].

Cervical cancer organoids can retain the histological characteristics, genetic characteristics, and tumor heterogeneity of the source tumor, thereby allowing the implementation of personalized treatment regimens based on the patient [100]. For the pathogenesis, drug screening, and efficacy prediction of female reproductive system malignancies, the preclinical tumor model based on the organoid platform helps us precisely select treatment options [120]. Although the advantages demonstrated by organoid technology have shown that it has broad potential in biomedicine, more exploration is still needed to improve the culture proto-

Table 2. Representative studies of cervical cancer organoids in precision medicine

Study Type	Research Focus	Key Findings/Applications	References
Drug Screening	High-throughput drug testing	Identified 7 compounds [from 171 candidates] with potent inhibitory effects on organoids.	[26]
	First-line chemotherapy response	Tested sensitivity of 4 cervical cancer organoid subtypes to standard chemotherapy regimens.	[91]
	Synergistic drug combinations	Propranolol [β-blocker] enhances trabectedin efficacy in HPV+ organoids.	[101]
	Targeted therapy validation	KRAS inhibitor (trametinib) and MYC inhibitor (MYCi975) show efficacy in small cell carcinoma organoids.	[102]
Radiotherapy	Radiosensitivity prediction	Organoids predict patient-specific radiation response and resistance mechanisms.	[105, 107]
	Mesenchymal component impact	Squamous-mesenchymal subtype organoids exhibit radioresistance due to glycolytic upregulation.	[106]
	Clinical validation	Organoid-predicted chemoradiation responses matched clinical outcomes in 2 advanced cases.	[109]
Immunotherapy	Adoptive T-cell therapy [ACT]	TTN mutations identified as predictors of ACT efficacy via organoid-T cell co-culture.	[114]
	γδT cell-mediated cytotoxicity	Organoid co-culture confirms γδT cell anti-tumor activity in cervical cancer.	[24, 115]
	Immune microenvironment modeling	Co-culture systems developed to evaluate PD-1/PD-L1 blockade and NK cell interactions.	[95]
Translational Models	Patient-derived xenograft (PDX) integration	Organoids maintain genetic stability post-transplantation into immunodeficient mice.	[103]
	Personalized treatment strategies	Organoid-guided therapy achieves 82% concordance with clinical outcomes in recurrent cases.	[98, 110]

Note: This table presents key research studies utilizing cervical cancer organoids for drug screening, radiotherapy, immunotherapy, and translational models. It highlights findings such as chemotherapy response testing, radiosensitivity predictions, immune microenvironment modeling, and personalized treatment strategies, demonstrating the clinical relevance of organoid-based approaches.

Table 3. Materials and characteristics of cervical cancer organoid technologies

Organoid Type	Scaffold Material	Key Growth Factors/ Cytokines	Pathological Subtype	Key Applications	References
Squamous Cell Carcinoma (SCC)	Matrigel (MBOC system)	RSPONDIN-1, Wnt3a, EGF, Noggin	Cervical SCC (70% incidence)	- Drug screening for cisplatin resistance - HPV integration analysis	[71-73]
Adenocarcinoma	Matrigel with sponge scaffolds	Nicotinamide, A-8301 (ALK inhibitor), PGE2	Cervical adenocarcinoma (25% incidence)	- KRAS/MYC inhibitor validation - Cystic tumor modeling	[75, 76]
Clear Cell Carcinoma	Fibrillar ECM scaffolds	FGF10, HGF, TGF-β inhibitor	Rare clear cell carcinoma	- HPV18 integration studies - Heterogeneity preservation	[38, 92]
Small Cell Neuroendocrine	Matrigel + collagen hybrid	KRAS pathway activators, MYC inhibitors	HPV18+ neuroendocrine carcinoma	- Targeted therapy screening (e.g., trametinib) - Radiation resistance mechanisms	[95, 102]
HPV-Related CIN/SCC	Air-liquid interface scaffolds	IL-2, IFN-γ, T cell activators	Precancerous lesions & invasive SCC	- HPV-driven EMT modeling - Single-cell analysis of premalignant cells	[27, 87]
Co-culture Models	Vascularized liver scaffolds	CAF-derived TGF-β, NK cell cytokines (e.g., IL-15)	Advanced/metastatic tumors	- Tumor-immune interaction studies - PD-1/PD-L1 blockade testing	[39, 95]

Note: This table details various cervical cancer organoid models, describing scaffold materials, key growth factors, pathological subtypes, and specific applications. Different models are tailored for drug resistance studies, HPV integration analysis, targeted therapy screening, and tumor-immune interaction assessments, providing insights into cervical cancer pathophysiology and treatment strategies.

col and integrate tumor parenchymal cells with the tumor stroma to restore the tumor microenvironment in the human body [121]. The organoid model is expected to build a comprehensive and complete cancer model system, providing an efficient research platform for tumor prevention, the selection of individualized treatment regimens, and the prediction of patient survival.

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Disclosure of conflict of interest

None.

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