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REVIEW PAPER

Advanced Organoid and 3D Bioengineered Platforms in Animal Biotechnology: Emerging Applications in Precision Livestock Farming and One Health

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ABSTRACT

Organoid and three-dimensional (3D) culture systems have emerged as transformative platforms in animal biotechnology by providing physiologically relevant alternatives to conventional two-dimensional (2D) cell cultures and experimental animal models. Derived from stem cells, organoids possess self-organizing capacity and closely mimic native tissue architecture, cellular heterogeneity, and organ-specific functions. Recent advances in extracellular matrix engineering, organ-on-chip systems, and genome editing technologies have significantly improved the stability, reproducibility, and translational relevance of organoid platforms.

In livestock biotechnology, organoids derived from cattle, pigs, sheep, and poultry are increasingly applied in disease modelling, host–pathogen interaction studies, reproductive biotechnology, and functional genomics research. These systems enable improved simulation of infectious and metabolic disorders while supporting precise evaluation of therapeutic responses and tissue-specific physiological mechanisms. Integration of CRISPR-Cas genome editing with organoid systems has further accelerated validation of genes associated with disease resistance, productivity, feed efficiency, and reproductive performance, thereby enhancing precision livestock breeding strategies.

Furthermore, integration of artificial intelligence, multi-omics technologies, and organ-on-chip platforms is expanding the predictive and translational potential of livestock organoids under the One Health framework. Despite limitations related to vascularization, immune integration, scalability, and species-specific standardization, continuous advancements in stem cell engineering and biofabrication are expected to improve future applications.

This review critically summarizes recent advances and emerging applications of organoid and 3D culture systems in disease modelling, functional genomics, precision livestock biotechnology, and sustainable veterinary research.

Keywords: - Organoid, 3D culture systems, Animal biotechnology, Livestock disease modelling, CRISPR-Cas genome editing, Organ-on-chip, Precision livestock biotechnology, Functional genomics, One Health

1. INTRODUCTION

Traditional animal biotechnology has long relied on two-dimensional (2D) cell culture systems and whole-animal experimental models to investigate biological processes, disease mechanisms, and genetic improvement strategies [1,2]. However, these conventional experimental approaches often fail to accurately reproduce the structural complexity, cellular heterogeneity, and physiological microenvironment of native tissues, thereby limiting translational relevance and predictive accuracy

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[2,3].

Recent advances in stem cell biology, biomaterials, tissue engineering, and microfabrication technologies have facilitated the development of organoids and three-dimensional (3D) bioengineered culture systems that closely mimic in vivo tissue organization and functionality [4-6]. Organoids are self-organizing multicellular structures derived from embryonic stem cells, adult stem cells, or induced pluripotent stem cells (iPSCs), capable of reproducing key structural and functional characteristics of their tissue of origin [5,7].

In animal biotechnology, organoid and 3D culture systems are increasingly being utilized for livestock disease modelling, host–pathogen interaction studies, reproductive biotechnology, regenerative medicine, toxicological screening, nutritional research, and precision livestock farming [6-9]. These advanced in vitro platforms provide physiologically relevant alternatives to traditional monolayer cultures and reduce dependence on animal experimentation [3,8].

Furthermore, integration of organoid systems with organ-on-chip platforms, bioprinting technologies, artificial intelligence-assisted modelling, and microfluidic devices has significantly improved the simulation of tissue-specific biochemical and mechanical environments under controlled conditions [4,9]. Recent developments in CRISPR-Cas genome editing and single-cell multi-omics technologies have further expanded the applications of organoid-based systems in functional genomics and translational veterinary research [8-10].

These innovations are expected to contribute substantially to One Health-oriented research by improving understanding of zoonotic diseases, antimicrobial resistance, animal welfare, food safety, and sustainable livestock production systems [9,10]. Therefore, organoid and 3D bioengineered platforms represent transformative tools in modern animal biotechnology research.
This review highlights recent progress in organoid and 3D bioengineered platforms in animal biotechnology, with emphasis on their emerging applications in livestock research, disease modelling, regenerative medicine, genome editing, precision livestock biotechnology, and One Health approaches [1-10].

2. LITERATURE SEARCH STRATEGY AND METHODOLOGY

Recent advances in organoid and three-dimensional (3D) culture technologies have significantly transformed modern biomedical and animal biotechnology research [11,12]. Traditional two-dimensional (2D) cell culture systems are limited in their ability to reproduce the structural organization, cellular heterogeneity, and physiological microenvironment of native tissues [12]. Consequently, researchers have increasingly focused on developing organoid and 3D bioengineered systems that more accurately mimic in vivo tissue architecture and function [13,14].

Organoids are self-organizing multicellular structures derived from stem cells that possess the ability to reproduce several structural and functional characteristics of native organs under controlled culture conditions [14,15]. These systems have demonstrated considerable applications in developmental biology, regenerative medicine, disease modelling, toxicological studies, and personalized medicine research [15,16].

Several studies have highlighted the importance of organoid technology in livestock and veterinary biotechnology. Animal-derived organoids have been successfully utilized for investigating intestinal infections, reproductive physiology, zoonotic diseases, vaccine development, and host–pathogen interactions [17,18]. Furthermore, organoid systems provide ethically acceptable alternatives to animal experimentation while improving experimental reproducibility and translational relevance [18].

Recent integration of organoids with organ-on-chip devices, microfluidic platforms, and bioprinting technologies has enhanced the physiological realism of these in vitro systems [19]. These advanced platforms allow dynamic nutrient exchange, mechanical stimulation, and tissue-specific microenvironment simulation under controlled experimental conditions [19,20]. Additionally, the incorporation of CRISPR-Cas genome editing and single-cell omics technologies has expanded the utility of organoid systems in functional genomics and precision livestock biotechnology research [18,20].

Despite these advancements, several challenges remain associated with organoid and 3D culture systems, including high production costs, variability in culture conditions, lack of vascularization, and limitations in long-term maintenance [16,19]. Nevertheless, continuous progress in biomaterials, tissue engineering, and artificial intelligence-assisted modelling is expected to further improve the reliability and applications of organoid technologies in animal biotechnology and One Health research [18-20].

3. RESULTS AND DISCUSSION

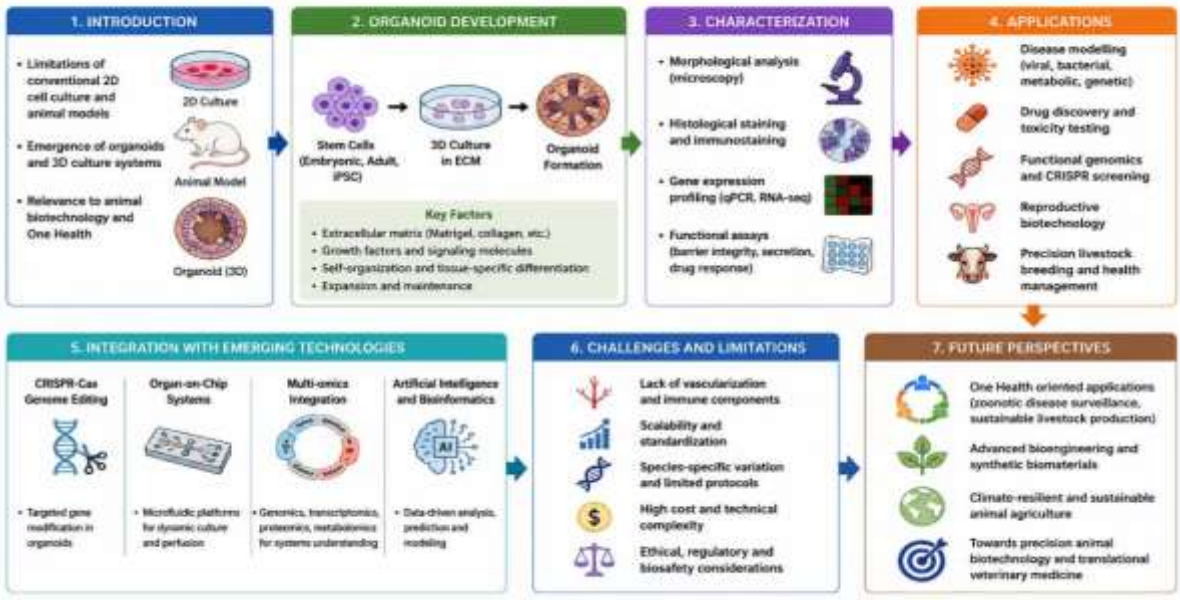
The collected literature demonstrates that organoid and three-dimensional (3D) culture systems represent a major advancement in modern animal biotechnology by providing physiologically relevant alternatives to conventional two-dimensional (2D) cell culture systems and experimental animal models. Unlike traditional monolayer cultures, organoids preserve tissue architecture, cellular heterogeneity, extracellular matrix interactions, and organ-specific functionality, thereby improving biological relevance and translational accuracy. Recent advancements in stem cell engineering, biomaterials, genome editing, organ-on-chip systems, and computational biology have significantly enhanced the stability, reproducibility, and applicability of livestock-derived organoids in disease modelling, functional genomics, reproductive biotechnology, and precision livestock improvement. Furthermore, integration of artificial intelligence and multi-omics technologies with organoid platforms has accelerated predictive veterinary research and sustainable animal production strategies under the One

Health framework. Collectively, these developments indicate that organoid systems are emerging as transformative tools in next-generation animal biotechnology and translational veterinary science [21-24].

Table 1. Comparison between conventional two-dimensional (2D) cell culture systems and organoid/three-dimensional (3D) culture systems in animal biotechnology

Parameters	Conventional 2D Cell Culture	Organoid/3D Culture Systems
Cellular organization	Monolayer growth of cells on flat surfaces	Self-organized multicellular three-dimensional architecture
Physiological relevance	Limited simulation of in vivo tissue environment	Closely mimics native tissue structure and function
Cell–cell interaction	Minimal and artificial	Extensive and physiologically relevant
Cell–extracellular matrix interaction	Poorly represented	Maintained through extracellular matrix support
Tissue polarity	Frequently absent	Preserved tissue polarity and organization
Cellular heterogeneity	Limited cell diversity	Maintains multiple cell types and heterogeneity
Differentiation potential	Reduced long-term differentiation	Enhanced differentiation and tissue-specific maturation
Gene expression patterns	Often altered under artificial conditions	More similar to native tissues
Disease modelling accuracy	Limited predictive capability	Improved modelling of infectious, metabolic, and genetic diseases
Host–pathogen interaction studies	Simplified interaction systems	More realistic simulation of infection biology
Drug screening and toxicity testing	Lower translational predictability	Higher physiological and pharmacological relevance
Functional genomics studies	Limited tissue complexity	Suitable for CRISPR-Cas functional genomics applications
Reproductive biotechnology applications	Restricted physiological simulation	Supports gametogenesis and reproductive tissue modelling
Long-term culture stability	Often limited	Improved self-renewal and maintenance capacity
Scalability and standardization	Relatively easy and cost-effective	Technically complex and expensive
Ethical considerations	Reduced animal usage compared with in vivo models	Further minimizes experimental animal dependency
Translational relevance	Moderate	High translational and clinical relevance
Major limitations	Poor tissue complexity and low physiological relevance	Vascularization, immune integration, and reproducibility challenges

Figure 1. Sectionwise Overview of Organoid and 3D Culture Systems in Animal Biotechnology



(FIG.1-Section wise overview of organoid and 3D culture systems in animal biotechnology, including organoid development, characterization, disease modelling applications, integration with emerging technologies, current challenges, and future perspectives.)

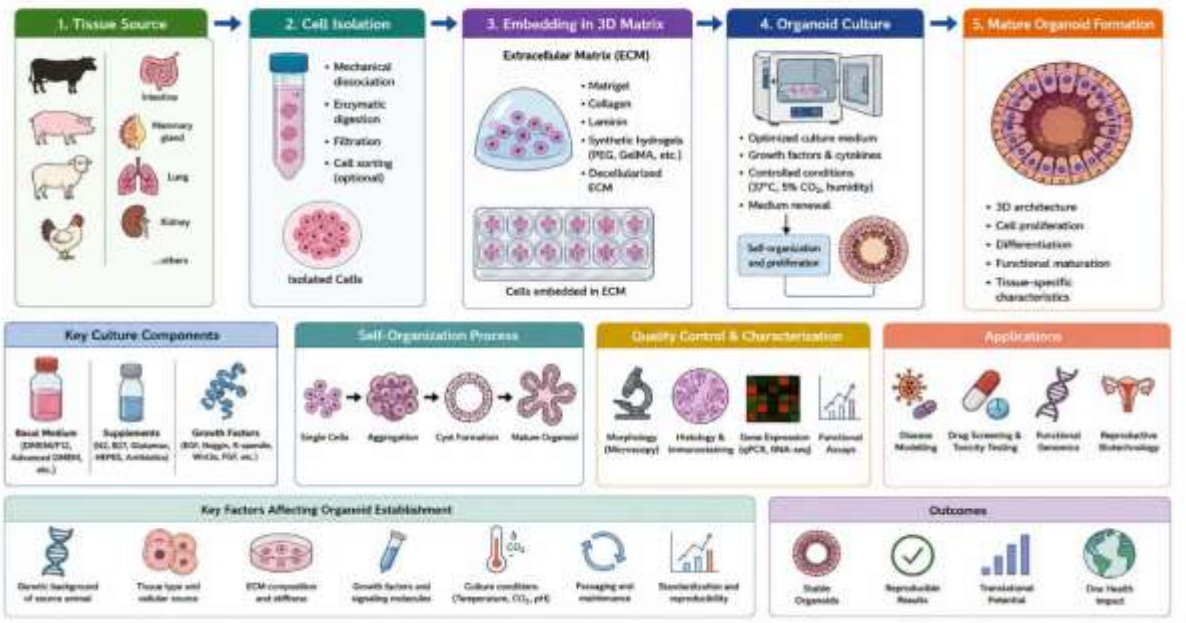
3.1 Evolution of Organoid and 3D Culture Systems in Animal Biotechnology

Recent advances in stem cell biology, tissue engineering, and regenerative biotechnology have positioned organoid and three-dimensional (3D) culture systems as transformative platforms in modern animal biotechnology. Conventional two-dimensional (2D) cell cultures have long been utilized for studying cellular physiology and disease mechanisms; however, they fail to accurately reproduce tissue architecture, extracellular matrix interactions, cellular heterogeneity, and organ-specific functionality observed under in vivo conditions. Consequently, traditional monolayer cultures often produce limited predictive accuracy in translational veterinary and livestock research. In contrast, organoid systems possess self-organizing capacity and maintain multicellular complexity, epithelial polarity, and tissue-specific differentiation patterns, thereby providing physiologically relevant experimental models with superior biological fidelity [21-23].

Organoids are primarily derived from embryonic stem cells, adult stem cells, or induced pluripotent stem cells and are cultured within extracellular matrix-supported environments that mimic native tissue microenvironments. Advances in biomaterial engineering and synthetic hydrogel technologies have substantially improved organoid stability, maturation, and long-term viability. Compared with conventional culture systems, organoids provide enhanced simulation of tissue development, metabolic regulation, and cellular communication pathways, thereby improving experimental reproducibility and translational relevance. Recent livestock-based organoid studies involving cattle, pigs, sheep, poultry,

and aquatic species further demonstrate their expanding significance in veterinary biotechnology and precision livestock research [24-26].

Figure 2. Schematic Overview of Organoid Development and Establishment in Animal Biotechnology



(FIG.2-Schematic overview of organoid development and establishment in animal biotechnology, including tissue collection, cell isolation, extracellular matrix embedding, organoid culture, self-organization, characterization, and translational applications.)

3.2 Applications of Livestock Organoids in Disease Modelling

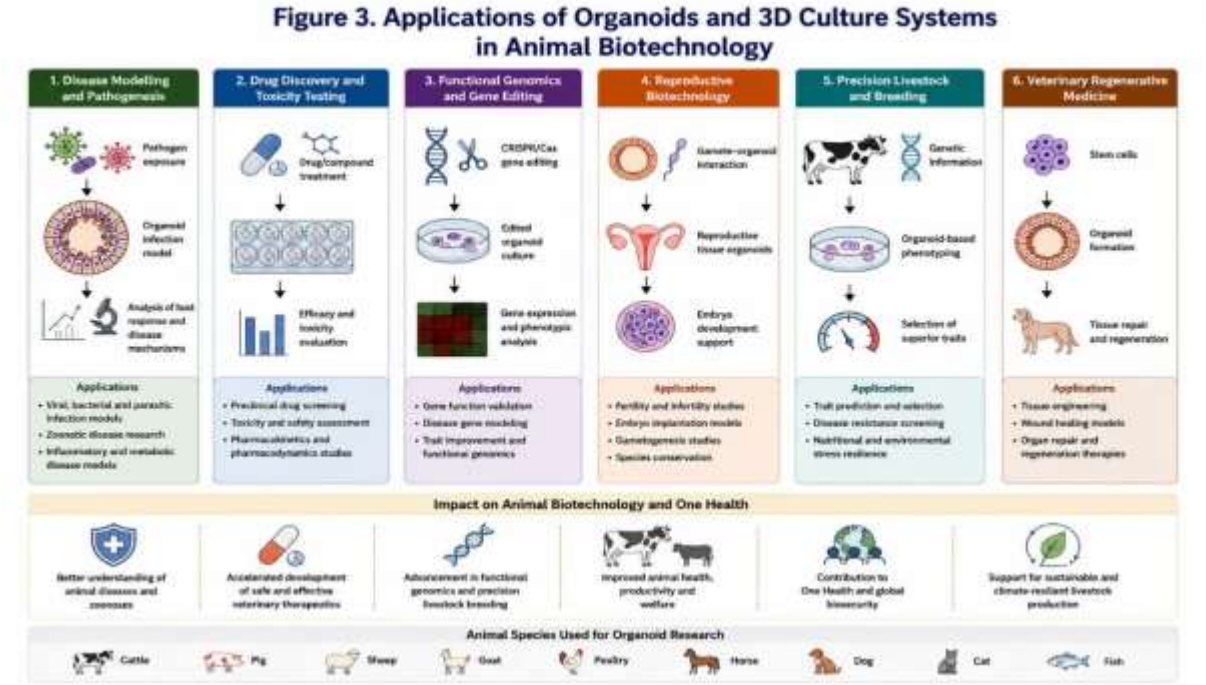
One of the most important applications of organoid technology in animal biotechnology is disease modelling and investigation of host–pathogen interactions. Livestock-derived intestinal, respiratory, hepatic, mammary, and reproductive organoids have demonstrated remarkable ability to replicate organ-specific infection dynamics and tissue responses under controlled laboratory conditions. Unlike conventional 2D cultures, organoids preserve epithelial integrity, tissue polarity, and multicellular interactions, enabling more accurate simulation of microbial colonization, viral replication, inflammatory signaling, and tissue regeneration processes [26-28].

Porcine intestinal organoids have been extensively utilized for studying enteric viral diseases such as porcine epidemic diarrhea virus, transmissible gastroenteritis virus, and rotavirus infections, whereas bovine respiratory organoids have shown high translational value for investigating respiratory pathogens associated with bovine respiratory disease complex. Similarly, avian intestinal organoids are increasingly applied in poultry disease research for understanding salmonellosis, coccidiosis, and avian influenza pathogenesis. These organoid systems enable real-time assessment of pathogen invasion mechanisms, immune signaling pathways, and therapeutic responses while significantly reducing dependence on experimental animals [27-29].

Furthermore, organoid-based infection models are increasingly recognized as critical tools for zoonotic disease surveillance under the One Health framework. Their ability to mimic species-specific tissue responses provides valuable insights into pathogen evolution, cross-species transmission, and host susceptibility mechanisms. Such translational applications are particularly relevant in the context of emerging infectious diseases affecting both livestock and human populations globally [29,30].

Table 2. Livestock-derived organoids and their major applications in animal biotechnology

Livestock Species	Organoid Type	Major Applications	Key Research Significance
Cattle	Intestinal organoids	Host–pathogen interaction studies, nutrient absorption analysis	Understanding gastrointestinal diseases and feed efficiency
Cattle	Mammary gland organoids	Lactation biology, milk protein synthesis, mastitis research	Improvement of dairy productivity and udder health
Cattle	Respiratory organoids	Bovine respiratory disease modelling	Investigation of respiratory pathogens and therapeutic responses
Pig	Intestinal organoids	Viral infection studies, toxicology, microbiome research	Modelling porcine epidemic diarrhea and enteric diseases
Pig	Hepatic organoids	Metabolic disorder studies and drug metabolism	Translational toxicology and precision veterinary medicine
Pig	Reproductive organoids	Fertility and reproductive biotechnology research	Embryonic development and reproductive efficiency studies
Sheep	Ovarian organoids	Follicular development and endocrine studies	Reproductive physiology and fertility improvement
Goat	Mammary organoids	Milk secretion and glandular development studies	Dairy biotechnology applications
Poultry	Intestinal organoids	Avian disease modelling and nutrient metabolism	Poultry health and feed conversion efficiency research
Poultry	Respiratory organoids	Avian influenza and respiratory pathogen studies	Zoonotic disease surveillance and infection biology
Fish/Aquatic species	Gill and intestinal organoids	Aquatic toxicology and environmental stress studies	Sustainable aquaculture biotechnology
Multi-species livestock models	Organoid-on-chip systems	Drug screening, precision livestock biotechnology	Advanced translational veterinary research



(FIG.3-Applications of organoid and three-dimensional (3D) culture systems in animal biotechnology, including disease modelling, drug screening, functional genomics, reproductive biotechnology, precision livestock breeding, regenerative veterinary medicine, and One Health-oriented translational research.)

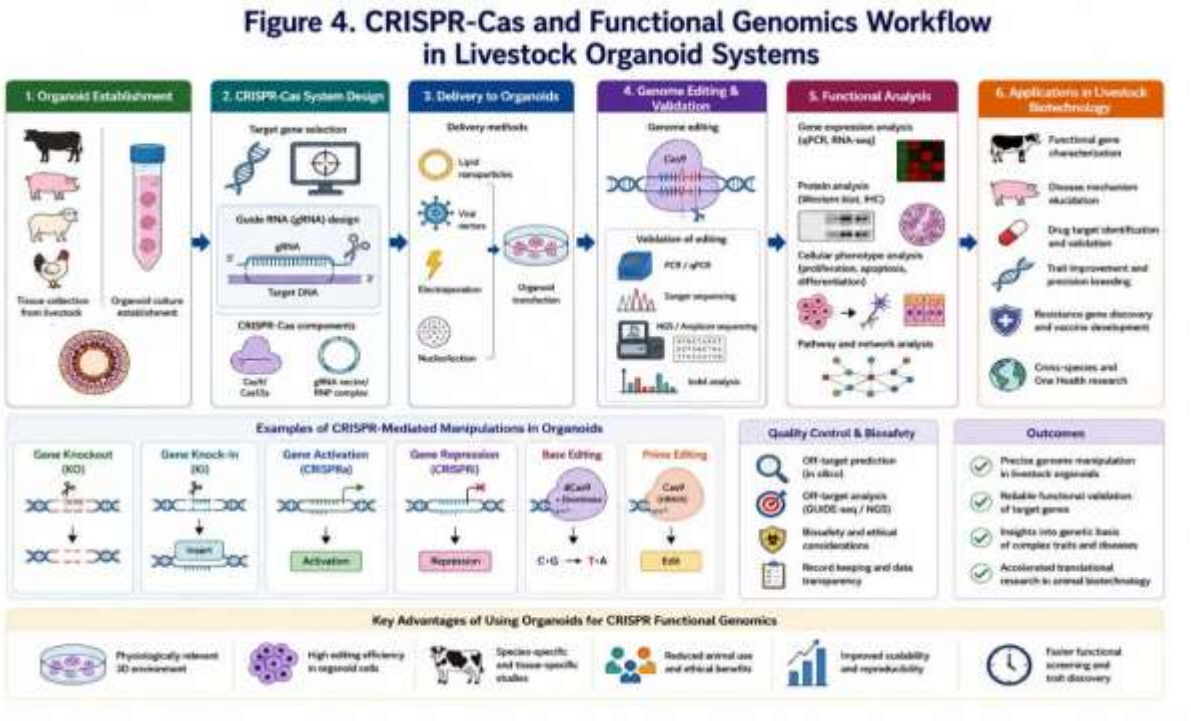
3.3 Integration of CRISPR-Cas Genome Editing with Organoid Platforms

The integration of organoid systems with CRISPR-Cas genome editing technologies represents a major breakthrough in precision livestock biotechnology and functional genomics research. Traditional livestock improvement strategies largely depend on long-term selective breeding and phenotypic evaluation, which are time-consuming and influenced by environmental variability. In contrast, CRISPR-integrated organoid systems allow rapid functional validation of genes associated with productivity, immunity, metabolic efficiency, reproductive traits, and disease resistance under physiologically relevant conditions [30-32].

Recent studies demonstrate that gene-edited intestinal and mammary organoids can effectively evaluate candidate genes associated with nutrient absorption, inflammatory regulation, milk production, and pathogen resistance in cattle and pigs. Similarly, reproductive organoids combined with genome editing technologies provide new opportunities for investigating fertility-associated genes and embryonic developmental pathways. These approaches substantially accelerate genomic selection programs and improve precision breeding efficiency in livestock species [31-33].

Importantly, CRISPR-organoid platforms reduce the need for extensive whole-animal experimentation by enabling early-stage screening of genetic modifications within controlled in vitro environments. This contributes to ethical biotechnology development aligned with the 3Rs principles of Replacement, Reduction, and Refinement. Despite these advantages, challenges such as off-target editing effects,

genomic instability, and species-specific editing efficiencies remain critical limitations requiring further investigation [32-34].



(FIG.4-CRISPR-Cas-mediated functional genomics workflow in livestock organoid systems, illustrating organoid establishment, guide RNA design, genome editing strategies, delivery methods, validation approaches, functional analysis, and translational applications in precision livestock biotechnology and disease modelling

3.4 Organoid Systems in Reproductive Biotechnology and Livestock Improvement

Organoid technology has emerged as a promising platform in reproductive biotechnology due to its ability to reproduce tissue-specific hormonal and structural characteristics more accurately than conventional reproductive cell cultures. Ovarian, uterine, placental, and testicular organoids are increasingly utilized for studying folliculogenesis, spermatogenesis, endocrine signaling, embryo implantation, and reproductive pathophysiology in livestock species [33-35].

These systems provide valuable opportunities for improving assisted reproductive technologies such as in vitro fertilization, embryo transfer, cloning, and germplasm preservation. Reproductive organoids also enable mechanistic evaluation of hormone-mediated signaling pathways involved in fertility regulation and embryonic development under physiologically relevant conditions. Consequently, organoid platforms may contribute significantly to improving reproductive efficiency, genetic conservation, and breeding performance in economically important livestock species [34-36].

Organoid systems facilitate investigation of reproductive diseases including endometritis, ovarian dysfunction, and placental abnormalities, which remain major causes of reduced livestock productivity worldwide. Their application in reproductive toxicology and endocrine disruption studies further

enhances their significance in veterinary biotechnology and sustainable animal production research [35,36].

3.5 Organ-on-Chip and Bioengineering Integration for Advanced Livestock Modelling

Recent integration of organoids with organ-on-chip technologies and advanced bioengineering systems has substantially improved the physiological relevance and translational applicability of livestock organoid models. Conventional static organoid cultures often experience limitations related to nutrient diffusion, oxygen availability, and waste accumulation, restricting long-term functionality and tissue maturation. Organ-on-chip platforms overcome these barriers by providing dynamic microfluidic perfusion, mechanical stimulation, and controlled biochemical gradients that more closely simulate in vivo physiological conditions [36-38].

Organoid-on-chip systems have demonstrated improved cellular differentiation, tissue organization, vascular-like functionality, and experimental reproducibility compared with conventional 3D cultures. These platforms are increasingly utilized for veterinary drug screening, toxicological evaluation, vaccine testing, and metabolic studies in livestock species. Furthermore, integration of biosensors and real-time monitoring systems enables continuous assessment of physiological responses and disease progression, thereby enhancing predictive accuracy in translational veterinary research [37-39].

Despite these advancements, standardization of chip design, biomaterial compatibility, and species-specific optimization remains a significant challenge for large-scale application. Nevertheless, continued progress in microengineering and bioprinting technologies is expected to accelerate development of highly complex multi-organ livestock-on-chip systems in the near future [38,39].

3.6 Artificial Intelligence and Multi-Omics Integration in Livestock Organoids

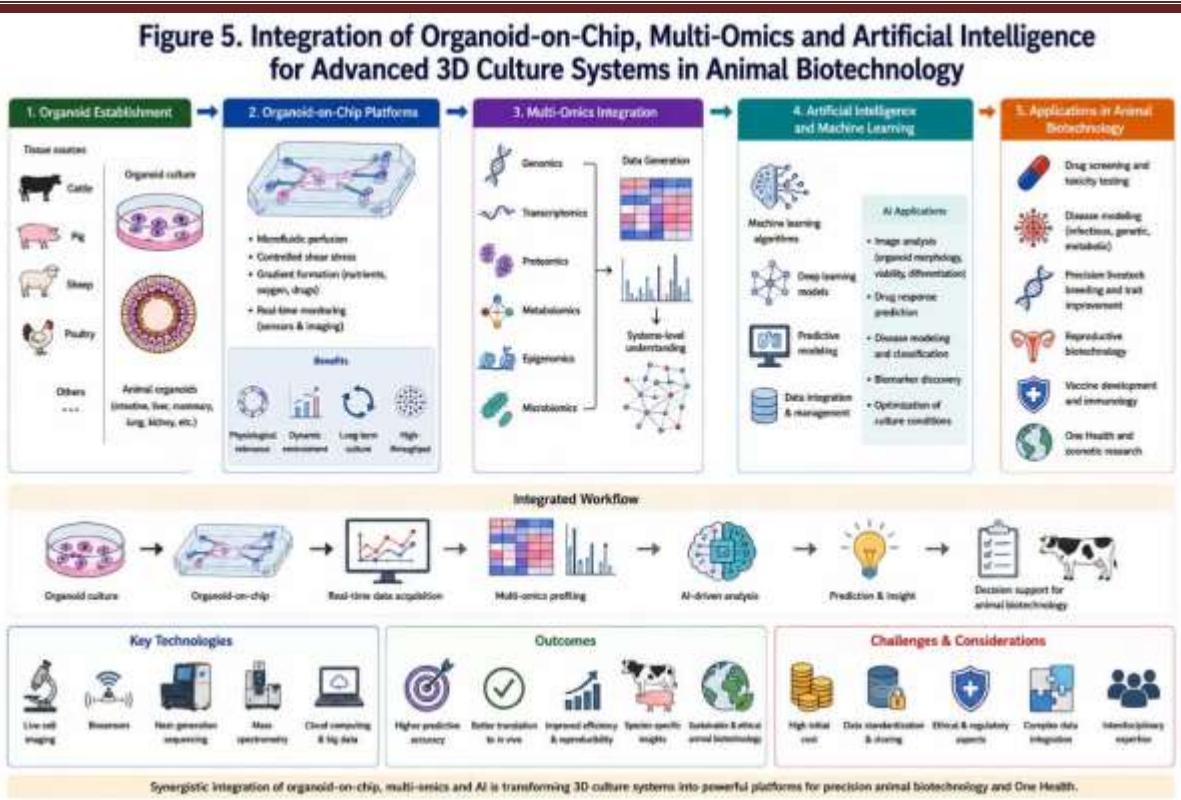
The convergence of artificial intelligence (AI), machine learning, and multi-omics technologies with organoid systems represents one of the most innovative developments in next-generation animal biotechnology. AI-assisted computational imaging enables automated analysis of organoid morphology, differentiation efficiency, tissue viability, and disease phenotypes with significantly improved precision and reproducibility compared with conventional manual assessment methods [40-42].

Simultaneously, integration of transcriptomics, proteomics, metabolomics, spatial transcriptomics, and single-cell RNA sequencing technologies has enhanced understanding of cellular heterogeneity and molecular signaling networks within livestock organoids. These approaches enable identification of biomarkers associated with feed efficiency, reproductive performance, stress adaptation, immune competence, and disease susceptibility in farm animals [41-43]. Single-Cell RNA Sequencing Computational Biology.

AI-integrated organoid platforms also support predictive modelling of therapeutic responses, pathogen susceptibility, and genetic performance, thereby contributing to precision livestock farming and digital veterinary health systems. Such interdisciplinary integration is expected to accelerate development of personalized veterinary therapeutics and highly efficient genomic selection strategies in livestock biotechnology [42,43].

Table 3. Integration of emerging technologies with organoid platforms in animal biotechnology

Emerging Technology	Major Applications in Organoid Systems	Advantages	Current Limitations
CRISPR-Cas genome editing	Functional genomics, disease-resistance studies, trait validation	Precise gene modification and rapid functional analysis	Off-target effects and editing efficiency variability
Organ-on-chip systems	Dynamic tissue modelling and microphysiological simulation	Improved physiological relevance and real-time monitoring	Complex fabrication and standardization challenges
Artificial intelligence (AI)	Automated organoid imaging and predictive analysis	Enhanced data interpretation and high-throughput screening	Dependence on computational infrastructure and datasets
Machine learning algorithms	Disease prediction and phenotypic characterization	Improved analytical accuracy and biomarker identification	Algorithm bias and limited biological datasets
Single-cell RNA sequencing	Cellular heterogeneity and lineage analysis	High-resolution molecular profiling	High cost and computational complexity
Spatial transcriptomics	Tissue-specific gene expression mapping	Improved understanding of spatial cellular organization	Technical limitations and data integration challenges
Proteomics	Protein expression and signalling pathway analysis	Functional molecular characterization	Sample preparation complexity
Metabolomics	Metabolic profiling and biomarker discovery	Improved understanding of cellular metabolism	Sensitivity and reproducibility limitations
Bioprinting technologies	Construction of complex tissue-like structures	Enhanced tissue organization and vascularization potential	High technical expertise and equipment cost
Synthetic biomaterials	Scaffold engineering and extracellular matrix replacement	Improved reproducibility and scalability	Limited biomimetic complexity
Biosensor integration	Real-time physiological and toxicological monitoring	Continuous assessment of organoid functionality	Sensor compatibility and calibration issues
Multi-organ chip systems	Simulation of systemic physiological interactions	Advanced translational modelling capacity	High system complexity and maintenance cost



(FIG.5-Integration of organoid-on-chip platforms, multi-omics technologies, and artificial intelligence in advanced 3D culture systems for animal biotechnology, highlighting data integration, predictive modelling, functional analysis, precision livestock applications, and One Health-oriented translational research.

3.7 Organoids in Climate-Resilient and Sustainable Livestock Production

Climate change-associated stressors including heat stress, oxidative damage, environmental toxins, nutritional instability, and emerging infectious diseases continue to negatively impact livestock productivity worldwide. In this context, organoid systems provide valuable experimental platforms for studying tissue-specific responses to environmental stress conditions under controlled laboratory environments [43,44].

Livestock organoids can be utilized to investigate cellular adaptation mechanisms associated with thermal stress, metabolic disruption, inflammatory responses, and toxin exposure. These studies may facilitate identification of stress-resilient genetic markers and support development of climate-adaptive breeding strategies for sustainable livestock production systems [44,45]. Furthermore, organoid technology contributes to environmentally sustainable biotechnology by reducing dependence on animal experimentation and minimizing biological waste generation.

Under the global One Health framework, organoid systems also provide integrated platforms for studying zoonotic pathogens and cross-species disease transmission dynamics linking animal, human, and environmental health systems [45,46].

3.8 Current Challenges, Research Gaps, and Future Directions

Despite substantial progress, several technical and biological limitations continue to restrict large-scale implementation of organoid systems in livestock biotechnology. Most currently available organoids lack functional vascularization, immune system integration, neural connectivity, and microbiome interactions, thereby limiting their ability to fully reproduce systemic physiological complexity. Variability in stem cell sources, extracellular matrix composition, culture conditions, and species-specific differentiation protocols further affects reproducibility across laboratories [46-48].

Long-term maintenance, scalability, cost-effective production, and industrial standardization remain additional barriers for commercial application in veterinary medicine and livestock breeding programs [47-49]. Furthermore, translation of in vitro organoid findings into whole-animal physiological performance remains complicated by gene–environment interactions, epigenetic regulation, and polygenic trait complexity.

Collectively, the convergence of organoid systems with CRISPR genome engineering, organ-on-chip bioengineering, artificial intelligence, and multi-omics analytics represents a transformative shift toward predictive and precision-based livestock biotechnology. These next-generation platforms are expected to redefine veterinary disease modelling, sustainable livestock production, functional genomics, and translational One Health research, thereby establishing organoid technology as a cornerstone of future animal biotechnology [48-50].

Table 4. Current challenges and future perspectives of organoid technology in animal biotechnology

Current Challenges	Impact on Organoid Research and Applications	Potential Future Solutions
Lack of vascularization	Restricted nutrient diffusion and limited tissue maturation	Development of vascularized organoids and bioprinting approaches
Limited immune system integration	Incomplete simulation of host immune responses	Immune-organoid co-culture systems and immunocompetent models
Absence of microbiome interactions	Reduced physiological relevance in gastrointestinal studies	Integration of microbiota-based culture systems
Species-specific variability	Poor reproducibility across livestock species	Standardized species-specific culture protocols
High culture cost	Limited large-scale and commercial application	Cost-effective synthetic biomaterials and automated systems
Limited scalability	Difficulty in industrial and high-throughput applications	Bioreactor-assisted large-scale organoid production
Genetic instability during long-term culture	Reduced experimental reliability	Improved stem cell quality control and monitoring systems

Technical complexity	Requirement for specialized expertise and infrastructure	Simplified standardized culture methodologies
Variability in extracellular matrices	Reduced reproducibility and experimental consistency	Synthetic and chemically defined matrix development
Ethical and regulatory concerns	Delayed translational and commercial implementation	Establishment of international regulatory guidelines
Limited long-term maintenance	Reduced experimental duration and functionality	Advanced nutrient perfusion and organ-on-chip integration
Data integration challenges	Difficulty analyzing multi-omics and AI-generated datasets	Improved bioinformatics and computational platforms
Incomplete organ-level complexity	Limited systemic physiological simulation	Multi-organ chip and interconnected organoid systems
Translational limitations	Difficulty extrapolating findings to whole animals	Integration of in vivo validation and precision modelling
Environmental stress sensitivity	Reduced organoid stability under variable conditions	Development of stress-resilient culture systems

4. CONCLUSION

Organoid and three-dimensional (3D) culture systems have emerged as transformative technologies in modern animal biotechnology by providing physiologically relevant and functionally superior alternatives to conventional two-dimensional cell cultures and experimental animal models. These advanced bioengineered platforms have significantly improved the accuracy of disease modelling, host–pathogen interaction studies, reproductive biology research, and functional genomics in livestock species. Compared with traditional in vitro systems, organoids better replicate tissue architecture, cellular heterogeneity, extracellular matrix interactions, and organ-specific physiological responses, thereby enhancing translational relevance in veterinary and comparative biomedical research.

The integration of organoid platforms with CRISPR-Cas genome editing, organ-on-chip technologies, artificial intelligence-assisted phenotyping, and multi-omics approaches has further expanded their application in precision livestock breeding, disease resistance studies, and sustainable animal production. These technologies collectively provide powerful tools for rapid functional validation of economically important traits and support the development of predictive livestock biotechnology systems.

Despite substantial advancements, several challenges including incomplete vascularization, limited immune system integration, species-specific variability, scalability constraints, and lack of standardized protocols continue to restrict large-scale commercial and translational application. Nevertheless,

ongoing progress in stem cell engineering, biofabrication, computational biology, and synthetic biomaterials is expected to overcome many of these limitations in the near future.

Overall, organoid and 3D culture technologies are poised to become foundational platforms in next-generation veterinary biotechnology, precision livestock farming, translational disease research, and One Health-based sustainable animal production systems [29,35,40].

5. FUTURE PERSPECTIVES

The future of organoid and three-dimensional (3D) culture systems in animal biotechnology is expected to be driven by the convergence of stem cell engineering, genome editing, artificial intelligence, multi-omics analytics, and advanced biofabrication technologies [16 ,36, 43]. Emerging developments in vascularized organoids, synthetic extracellular matrices, and bioprinting are likely to improve tissue complexity, physiological functionality, and long-term stability of livestock-derived organoid systems.

Integration of CRISPR-Cas genome engineering with organoid platforms will further accelerate functional genomics research and enable rapid identification of genes associated with disease resistance, reproductive efficiency, feed conversion, stress tolerance, and climate adaptability in livestock species [7,20,31,35]. Similarly, incorporation of artificial intelligence and machine learning approaches into organoid analysis is expected to enhance automated phenotyping, predictive disease modelling, and precision breeding strategies [24,40,41].

Future development of interconnected multi-organ livestock-on-chip systems may enable accurate simulation of systemic physiological processes including immunity, metabolism, endocrine regulation, microbiome interactions, and toxicological responses under controlled laboratory conditions [17,25,27,28]. Such platforms could revolutionize veterinary drug development, vaccine testing, nutritional research, and translational livestock biotechnology.

Furthermore, organoid systems are expected to play a major role in climate-resilient livestock production and zoonotic disease surveillance under the global One Health framework. Their ability to reduce dependence on experimental animals while improving predictive biological accuracy supports sustainable and ethically responsible biotechnology development [12,46].

Collectively, the integration of organoid systems with next-generation computational and bioengineering technologies is expected to redefine the future of precision animal biotechnology, sustainable livestock farming, and translational veterinary medicine [19,29,30,36].

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