American Journal of Machine Learning

australiansciencejournals.com/ml

E-ISSN: 2689-0003

Volume 7 issue 1 2026

Application Research Progress and Prospects of Organoid Models in Individualized Metabolism Studies

Hongxuan Li
Guangxi University of Chinese Medicine, Nanning, 530200,Guangxi, China
First author:3385874884@qq.com(Hongxuan Li)
Zheyi Xu
Guangxi University of Chinese Medicine, Nanning, 530200,Guangxi, China
Xiaoying Qu
Guangxi University of Chinese Medicine, Nanning, 530200,Guangxi, China
Bojia Li
Guangxi University of Chinese Medicine, Nanning, 530200,Guangxi, China
Yanhui Cen
Guangxi University of Chinese Medicine, Nanning, 530200,Guangxi, China
Correspondence author:*1316133198@qq.com(Yanhui Cen)*

Abstract: *To review the application of organoid models in individualized metabolism research and evaluate their value in disease modeling and personalized drug screening.*

Methods: *Relevant literature on organoid technology and metabolomics was systematically reviewed. Studies integrating organoid culture with analytical techniques such as nuclear magnetic resonance (NMR) and mass spectrometry (MS) were analyzed to summarize current research progress and technical challenges.*

Results: *Organoid models, especially patient-derived organoids (PDOs), can recapitulate the three-dimensional structure, cellular composition, and genetic characteristics of original tissues. Combined with metabolomics technologies, they provide an effective platform for studying metabolic heterogeneity, disease mechanisms, and individualized drug responses. Organoids have been widely applied in tumor metabolism research, metabolic disease modeling, and high-throughput drug sensitivity testing. However, challenges remain, including incomplete simulation of the in vivo microenvironment, variability in culture systems, limitations in metabolic detection technologies, and lack of standardized protocols for clinical translation.*

Conclusion: *Organoid technology provides a promising in vitro model for individualized metabolism research. With advances in multi-omics integration, artificial intelligence analysis, and multi-organ systems, organoid platforms are expected to play an increasingly important role in precision medicine and personalized metabolic therapy.*

Keywords:*: Organoid models, Personalized metabolism, Precision medicine, Drug metabolism studies, Patient-derived organoids, Metabolic disease modeling, Pharmacokinetics, In vitro disease models.*

1. Introduction:

The fundamental means of the maintenance of life activities is metabolic homeostasis. It has been indicated that the pathogenesis and response to treatment against different major infections, including cancer, diabetes, non-alcoholic fatty liver disease, and neurodegenerative diseases, is intimately linked to an individual metabolic malfunction[0]. Nevertheless, in the traditional metabolic studies, classical models have serious defects in being able to recap the intricate tissue framework, cell-cell relations and genetic backgrounds unique to a particular individual of a human being. It significantly prevents the comprehensive investigation and study of disease metabolic heterogeneity, the development of an individual approach to treatment. The development of organoids as a new breakthrough in biomedical research occurs relatively quickly over the recent years. Organoids are small analogs made in vitro of an organ through self-assembly of pluripotent stem cells or tissue-specific adult stem cells in three-dimensional culture condition. They are able to seriously recreate the structure of tissues, type of cells and the most important physiological functions of the source organ[0]. It has been demonstrated that the technology since the successful creation of the first intestinal organoid in 2009 has spread to other organs including the liver, brain, kidney, and pancreas along with their respective tumor tissues, offering an unparalleled disease modeling, drug screening, and regenerative medicine platform[0]. Even though the potential of organoids in research is immense, many challenges and obstacles still exist in the application of organoids, such as stability of models, standardisation of metabolic detection technologies, complexity of integration of multi-complex microenvironment, clinical routes of translation[0]. The current article will use a systematic review of literature related to the application of the organoid models in individualized metabolism studies, thoroughly investigate the recent successes of the models in examining tumor metabolic heterogeneity, elucidating the mechanisms of metabolic diseases, and guiding personalized drug screening, examine the current challenges of interest, and predict the future trend of the development of the models, with hope that all will serve as a reference to the development of precision metabolic medicine.

2. Theoretical Basis of Organoid Models and Individualized Metabolism Research

2.1 The Connotation and Practical Needs of Individualized Metabolism Research

Individualized metabolism research aims to reveal unique metabolic phenotypes by systematically analyzing the overall changes of endogenous small-molecule metabolites in individuals under specific physiological or pathological states, thereby providing corresponding basis for precise disease early warning, diagnosis, subtyping, and treatment[0]. Its core lies in recognizing that metabolism is the terminal link connecting genotype and phenotype, capable of dynamically and comprehensively reflecting the results of interactions among genetic background, environmental exposure, and lifestyle[0]. Metabolomics, as a key technology in this research, can detect thousands of metabolites in biological samples like blood and urine with high-throughput and high sensitivity using techniques such as nuclear magnetic resonance (NMR) or mass spectrometry (MS), showcasing an individual's unique metabolic phenotype[0]. The practical need mainly stems from the tremendous pressure faced by current clinical practice and disease research. Clinically, significant metabolic heterogeneity exists in major chronic diseases like cancer and cardiovascular diseases, making the effectiveness of traditional uniform, protocol-driven treatment plans very limited and challenging to precisely provide the most effective and targeted treatment for each patient[0]. For instance, the human health and disease metabolome atlas mapped by the research team led by Jin-Tai Yu from Fudan University revealed extensive associations between plasma metabolites and over a thousand diseases. It also found that metabolic changes could appear up to a decade before disease diagnosis, indicating that each patient has a unique individual condition

and highlighting the great potential of the metabolome as a biomarker for early diagnosis and risk prediction[0]. Furthermore, there are significant individual differences in drug efficacy and adverse effects, closely related to individual activity of drug-metabolizing enzymes, transporter expression, etc. Metabolomics can help understand individual metabolic responses under drug intervention, providing guidance for developing personalized medication regimens and dose adjustment[0]. Therefore, individualized metabolism research is a path to evolve from "one-size-fits-all" to "precision," aiming to achieve early intervention and personalized treatment for individual diseases by identifying individual-specific metabolic features[0].

2.2 Construction of Organoid Models and Their Individual-Specific Advantages

Organoids are scaffold-free microscale analogs of organs that are created in vitro by autogenic or patagonic differentiation (self-organization) of pluripotent stem cells or tissue-specific adult stem cells cultured under three-dimensional conditions. Their generation is generally by placing stem cells or tissue fragments into a scaffold with high levels of extracellular matrix and releasing them into medium, which contains component growth factors and cellular signaling inhibitors, which assumes control of the microenvironment in vivo and results in the development of a complex three-dimensional structure with major cell types, spatial structure, and partial functions of the original organ[0]. The best part of organoid models in the individual research is their specificity. The genetic and phenotypic property of a donor individual can be maximally retained in Patient-Derived Organoids (PDOs)[0]. Research has established that PDOs are very similar to the original tumor tissue of the parent in histomorphology, major protein expression, genomic mutation pattern, and transcriptome characteristics[0]. This is a very high level of fidelity that makes the organoids of each patient an ideal research surrogate of the disease that is theirs. Moreover, there is also an increased benefit of organoid technology to control culture and clinical translation value. In vitro culture conditions can be carefully manipulated by the researchers to recapitulate various phases of the disease process. More significantly, a small-size sample tissue of the patient can be cloned to a great number of PDOs in a few weeks, which can be used in a high-throughput drug sensitivity analysis. This enables drugs to be pre-tested on the patient in vitro to predict their clinical efficacy and give some alternatives in the way patients could be treated individually[0].

2.3 Applicability and Technical Foundation of Organoids in Metabolism Research

Since organoid models are capable of recreating the three dimensional architecture and cell interactions of the in vivo organs, it offers a platform that is akin to the physiological environment of patients in study of the organ specific metabolic functions and diseased condition[0]. Their usefulness can occur at various scales: liver organoids are the perfect tool to understand genetic factors and their contribution to molecular processes involved in different diseases such as alcohol-related liver disease (ALD), viral hepatitis, and liver cancer[0]; pancreatic organoids can be used as ideal models to study insulin secretion and response to drugs in diabetes[0]; brain organoids can be used to study the mechanisms of pathogenesis and abnormalities in energy metabolism and mitochondrial dysfunction in neurodegenerative diseases[0]; and tumor organoids can recapitulate the heterogeneity and reprogramming of tumor metabolism[0]. The basis of organoid metabolism studies on a technical level depends mainly on the integration of high-performance metabolomics analysis methods with organoid culture and functional evaluation methods. The key analytical techniques are targeted analysis and the untargeted analysis[0]. Most studies in metabolomics involve the use of various complementary analysis methods in order to achieve a more complete coverage and NMR and MS are the two fundamental platforms complemented in most cases by separation methods.

NMR Technology: NMR studies the structure of metabolites through observing the magnetic resonances of atomic nuclei within molecules. It is a high-throughput, rapid, non-destructive method and minimal sample preparation is needed, and it can even be applied to tissue analysis directly. Its primary disadvantages are that it is usually less sensitive than MS and signal multiplicity and overlap may present a challenge in the quantitative analysis[0].

MS Technology: "Untargeted or targeted metabolite analysis of organoid extracts can be done using metabolomics platforms, such as liquid chromatography-mass spectrometry (LC-MS), or gas chromatography-mass spectrometry (GC-MS), which thoroughly measure changes in their metabolites[0] or can be performed on no fewer than 100 analytes at once[0].

High-Resolution and Spatial Analysis Techniques: To circumvent the small-scale size shortcoming of organoids, miniaturized mass spectrometry examination techniques have been created to disclose large-abundance metabolites in small human liver organoids, displaying extensive metabolite heterogeneity among the organoids of different individuals[0]. The technique of spatial metabolomics imaging is able to map the location of the particular metabolites maintaining the spatial arrangement of the organoids, and capable of analyzing spatial metabolic gradients[0].

Combination of Functional and Mechanistic Studies: Organoid models can be used in combination with genetic editing to determine how certain genes affect metabolic pathways [28]. As an example, by knocking out the SIRT5 gene in pancreatic cancer organoids and intrigued with metabolomics analysis, SIRT5 gene was promoted glutamine metabolic rejuvenation by increasing the GOT1 enzyme activity, thus uncovering a novel tumor metabolic pathway and treatment regimen[0].

3. Application Progress of Organoid Models in Individualized Metabolism Research

3.1 Study of Metabolic Heterogeneity and Drug Response in Tumor Organoids

The use of Patient-Derived Organoids (PDOs) has turned into an effective tool to study tumor heterogeneity and predict drug response since it is able to recreate the histoarchitecture, genetic background, and molecular features of primary tumors to a great extent. Organoid models have proved to have considerable benefits in maintenance of intra and inter tumor heterogeneity. Just like patient-derived xenograft (PDX) models, tumor organoids have a high similarity the parental tumor; the models share epigenetic/genetic changes, histopathology, and sensitivity to anti-cancer drugs[0]. This makes organoids high fidelity and enables the use of organoids as a surrogate of patient tumors in in vitro studies. To illustrate this example, it is confirmed that organoids which are mechanically created using patient tumor tissue can mirror both morphological and genetic items of the original tumor, and these properties could be preserved despite long-term culture[0]. This gives high likelihood of in vitro experiments of tumor cell population with varying molecular subtypes, driver mutation, and metabolic phenotype. The prediction of responses to the clinical drug is yet another utility of organoids since it allows tailoring the drug regimen specifically on a patient. Evidence has been provided in the studies on PDX models that their sensitivity to conventional chemotherapeutic agents is strongly linked to the clinical outcomes of patients[0]. Based on this idea, the tumor organoids are extensively utilized in testing drug sensibilities. It can be determined which specific drug or combination of drugs could be beneficial to a certain patient by creating patient-specific organoids biobanks and performing high-throughput drug screening to identify the positive results. The in vitro method of drug testing is useful in identifying possible solutions to patients who do not respond to conventional treatment[0]. Even though various retrospective studies have indicated the positive association between organoid drug sensitivity

outcomes and patient clinical response, this clinical application as predictive biomarkers needs to be validated using large-scale prospective studies[0].

3.2 Exploring Mechanisms of Metabolic Abnormalities in Metabolic Disease Organoid Models

Organoid provides an unprecedented platform to make the modeling of the pathophysiological mechanisms of more complex metabolic diseases feasible.

In liver metabolic diseases, in 2025, Igarashi et al. were able to produce human adult hepatocyte organoids, which have long-term self-renewal ability and also full metabolic functions (including the production of bile acids, metabolism of drugs, gluconeogenesis)[0]. Through gene editing, functional simulated inherited metabolic liver diseases can be performed using such models. The major phenotypes of metabolic dysfunction-associated steatohepatitis (MASH) such as activation of pro-inflammatory pathways, lipid aggregation, and hyper-apoptotic sensitivity can be reproduced with the help of liver organoids of patient origin or induced by metabolite can be used to test the effectiveness of drugs such as metformin, L-carnitine, and FGF19 analogs[0]. Intestinal metabolism and immune interaction Patient-derived colon organoids have been utilized to identify epithelial cell-autonomous metabolic impairments in pediatric ulcerative colitis (UC). In the studies it was found that colon organoids of children with active UC had differentiation defects and hypermetabolic phenotype. The underlying cause is with normal activation of the peroxisome proliferator-activated receptor alpha (PPAR-AL)-mediated lipid metabolic reprogramming. This is one of the most significant basic instruments of exploration since organoids can clearly examine the effects of the epithelial cell metabolism as an independent disease determinant in the absence of immune cell and other microenvironment interactions[0].

Complicated interactive circulations in multi-organ, multi-system metabolic syndromes are also comprehended using organoid models. The functional roles of various parts can equally be segregated by corresponding organoids to give an opportunity to in-depth studies of the complex multi-system cooperation in the human body.

3.3 Application of Organoids in Individualized Metabolic Intervention and Drug Screening

The fundamental clinical translation value associated with organoid models is that it can be used to direct personalized metabolic intervention and drug screening, which results in personalized precision medicine. The first international expert-based consensus regarding organoid-based drug sensitivity testing was published in 2024, organizationally led by Academicians Yeguang Chen and Shaorong Gao, and it gives principle guidelines on how to standardize drug sensitivity testing (DST) using patient-derived organoids (PDOs)[0]. That year, the first group standard of China, which was titled, Technology for Drug-induced Liver Injury Evaluation Based on Human Liver Organoids, was officially launched to bring about the standardization of drug hepatotoxicity evaluation. The 2024 version of the Chinese Anti-Cancer Association (CACA) Guidelines) on glioma specifically mentioned the use of organoid models as an in vitro drug sensing platform to identify individualized chemotherapy in clinical practice. The predictive capability of organoids to clinical drug response means that they can be used as disease surrogates in patients in order to screen potentially effective treatment regimens in high-throughput DST in vitro. The results of the retrospective studies reveal positive correlation between organoid-based drug sensitivity and patient clinical treatment response[0]. Over the past years, organoid systems have become more sophisticated and can incorporate additional intricate stromal and immune models to test the efficacy of immunotherapy[0]. One of the breakthroughs is the air liquid interface (ALI) culture, which has the potential to grow PDOs using patient biopsy tissue. These organoids also have tumor epithelium as well as are naturally inscribed with a number of endogenous, homologous tumor

tumor-infiltrating lymphocytes (TILs) such as T cells, B cells, NK cells, and macrophages that fully retain the native tumor immune microenvironment[0]. In addition to direct guidance of patient treatment, organoids may be applied to the determination of new therapeutic targets and new compounds[0]. They are a good in vitro model to study tumorigenesis and cancer progression and show high potentials as translational research[0]. Moreover, the acquired resistance mechanisms can be best studied using organoid platforms and can be used to establish the mechanisms and effectiveness of combination therapies, which can offer new approaches to beating clinical drug resistance[0].

4. Challenges in Individualized Metabolism Research Using Organoids

4.1 Model Stability and Representativeness Issues

Major issues that define the feasibility of an organoid model in the study of metabolism are the stability of organoid models and their utility level in replicating the complex physiological environment in vivo. The majority of the existing organoid models are not able to recapitulate the entire cell types, innervation, vascular networks, and dynamic mechanical and electrochemical signaling microenvironment of existing organs[0]. One such example is liver organoids are often incompetent of the bile ducts, vascular networks, and other hepatic structures and can only detoxify the liver by 20-30 percent the activity of a native liver, reducing their usefulness in drug metabolism and toxicity investigations[0]. This simplified models used in metabolism studies find it difficult to dynamically supply nutrients in vivo, hormonal systemic regulation, and inter-organ metabolic axis interaction resulting in dissimilarities between in vivo and in vitro metabolic phenotypes thereby limiting reliability and biomimicry. Gross variability and reproducibility problems also were observed in organoid culture, in both batch-to-batch and in batch time advancement. Even minor variations in cell source, matrix materials, medium formulation and culture conditions, could result in an order of magnitude difference in organoid morphology, cellular composition, proliferation rate and metabolic function both between different labs or even between batches of the same lab[0]. Additionally, through extended periods of passage, organoids can experience genetic drift or selective proliferation of specific cell subpopulations, which would lead to a gradual divergence between them in genetic and metabolic properties of the original tissue, and therefore, the stability of long-term studies and the comparability of results[0].

Moreover, numerous organoids, particularly the ones based on pluripotent stem cells, tend to be immature or in a so-called fetal-like condition, which is not yet as functional as the adult organ would be[0]. This functional immaturity restricts their use in the study of adulthood of metabolic diseases.

4.2 Limitations in Metabolic Detection and Data Interpretation

Various metabolomics analysis methods severely differ in their levels of sensitization. Individually, MS technology with a combination of chromatography is highly sensitive, and can be used to detect low-abundance metabolites and forms relative identifications of metabolites within a relatively short period[0]. Conversely, the lack of sensitivity is one of the biggest limitations of NMR technology[0]. This is a difference in sensitivity that causes NMR to be difficult in the detection of low-concentration metabolites. More to the point, Physicochemical properties of metabolites are highly diverse and the biological systems are too complex to necessitate one detection technique to address and soften the whole metabolome[0]. The use of GC-MS and LC-MS tends to complement MS even in the context of the more comprehensive and clear data. This means that two or more methods of detection are likely to give improved results when used in untargeted studies in order to gain a more holistic view of the biological system of a person. However, the need of several technological platforms exerted considerable strain on the technical complexity

and cost of organoid metabolic detection, which prevents any large scale application. To investigate the heterogeneity of organoids in terms of their functional variants in the three-dimensional structure, it is essential to study their spatial distribution, which involves the aid of special imaging technology. Spatial distribution of metabolites can be obtained by mass spectrommetry imaging (MSI) such as desorption electrospray ionization mass spectrometry (DESI) techniques. Nevertheless, these spatial metabolomics technologies are generally difficult to use, expensive, and low throughput that leads to their challenge of generalisability in a normal organoid analysis approach. However, most metabolomics experiments to date continue to use the procedure of homogenizing the complete tissue or organoid prior to detection. The approach entirely eliminates the information on the spatial distribution heterogeneity of metabolites, and it will not allow to distinguish the metabolic state differences between different regions or different cell types in the organoid. The multidimensionality and heterogeneity of organoid metabolic data across space is very challenging to bioinformatics analysis. To be able to associate changes in metabolic fluxes measured as well as changes in metabolic concentrations with particular physiological processes or the pathological mechanisms in the pathology of disease more extensive databases of metabolic pathways and computational models are to be constructed. Furthermore, separation of disease-specific metabolic effects and effects of various culture conditions or their specific effects is a significant challenge and it is difficult to align different conditions and outcomes. In spite of the fact that artificial intelligence and machine learning algorithms are employed in order to process large amounts of data, the transparency and biological interpretability of these models continue to experience enhancement[0].

4.3 Standardization and Clinical Translation Challenges

In order to make a successful shift of organoid metabolism research out of the laboratory and into the clinic, the major issues of standardization creation and strict regulation should be solved. The absence of a single standardized research system is a significant barrier to the inability to apply the research of organoid metabolism broadly. Presently, the industry standards and operating guidelines relating to tissue obtaining and processing, choice of matrix material, medium development, culture settings and endpoint operating examines are deficient worldwide[0]. As discussed, various culture circumstances may produce varied outcomes and therefore such technical variability will render data of various research institutes can hardly be compared and combined on horizontal levels, drastically impacting the reproducibility and the credibility of the research results. Though, relevant group standards have already started to be published both locally and internationally[0], international-level cohesive standards are still not established[0]. There is still an unstable state regarding a comprehensive and unified system of the standard system over different organoids and different scenarios of application. Even under a relatively simple unified standard system, no obvious clinical translation route and regulatory scheme exists. A clinical use of organoids as a personalized therapy choice-making instrument remains in the infantile phase of exploration, without any established regulatory approval measures and clinical validation criteria. Though a major change happened in the international regulatory landscape in 2025, with China, the United States and other nations adopting the appropriate legislation and specifications, clearing the pathway and avenues to the clinical research of organoids[0], the predictive efficacy of the model to patient still needs confirmation through large-scale prospective clinical studies, which requires extensive preparation time, and immense amounts of money.

5. Development Prospects and Future Directions

As a life science, organoid technology is a highly innovative field of study that is rapidly transitioning out of laboratory research into clinical translation and industrialization. The

opportunities of its development in the sphere of the research of individual metabolism are specifically extensive, as they relate to many other aspects and combine with other technologies to develop constantly. Regulatory bodies worldwide are building policy frameworks to enable the advancement of the technology of organoid, being an effort to overcome barriers to clinical translation of organoid technology. The National Medical Products Administration (NMPA) Center for Drug Evaluation (CDE) of China published the first document to explicitly indicate that the use of data obtained via organ-on-a-chip/organoid using human cells can be used as compliant non-clinical data when seeking Investigational New Drug (IND) status in rare diseases regardless of the policy barrier of using animals in drug development. At the international level, the acceptance of regulations is quickening[0]. The U.S. “FDA Modernization Act 3.0" will diminish unwarranted animal research and clearly welcomes the emergence of fresh approach condition methodologies (NAMs) such as organoids and organ-on-a-chip[0]. The indicated policy adjustments indicate that the applications of organoids in research continue to receive international interest and shift to compliant data, thus offering a sound institutional basis of organoids in biomedical research and personalized research on metabolism. With the advent of the age of AI, its organizational and computation strengths can dramatically reduce the time period and enhance accuracy of the study of an individualized metabolism detection on the basis of organoid models. The profound adoption of AI in the multi-omics technologies is transforming the study concept and scope of application of organoids. Su suggested a rather innovative idea of the creation of digital copies of the organoids in the virtual reality, which they called Artificial Intelligence Virtual Organoids (AIVOs)[0].This technology integrates multimodal data like high-content imaging and single-cell omics, employing hybrid modeling strategies to achieve reversible, spatiotemporally continuous simulation and prediction of organoid development, disease progression, or drug response, providing new solutions for virtual high-throughput screening and clinical decision support[0]. Leveraging AI's excellent computational power, AI algorithms are being used to optimize complex parameters in organoid culture, automatically analyze vast amounts of morphological and functional data, and predict drug responses. Tan developed the world's first AI model for liver organoids, achieving classification prediction of unknown drug-induced liver injury levels by dynamically monitoring organoid morphological changes[0]. Furthermore, integrating metabolomics, proteomics, spatial transcriptomics, and other multi-omics technologies with organoid platforms via AI can construct a complete research sequence from structural analysis to functional prediction, achieving a closed loop. This will greatly reduce the time and economic costs of analysis and prediction, providing practical feasibility for in-depth individualized metabolic analysis and personalized treatment plans for more patients. On a technical basis, the normal function of various organs relies on vascular networks, but the lack of vascularization is a major obstacle limiting organoid maturation and function. In 2025, Miao successfully created the first lung organoids with an organotypic vascular network, achieving co-development of lung tissue and vasculature, significantly enhancing cellular diversity, 3D structure, and functional maturity[0]. Abilez et al. also successfully used micropatterned human pluripotent stem cell-derived gastruloids to simulate, for the first time in vitro, the early vascularization process of the human heart and liver[0].Such innovations can enhance the ability of organoids to capture such processes as transporting nutrients and clearance of metabolic waste products, and represent a stronger basis towards simulating multi-organ interactions. Even in the future, organoid models will surely go beyond single organ simulations, and will evolve to more intricate and systemic forms. The control of the metabolism is a team play worn out by several organs, rather than a one-man show played by an individual organ. Thus, organoid simulations also require developing respective interactive axes to carry out joint

experiments. Tao et al. have created a microfluidic liver-islet organoid interaction chip, in which human induced pluripotent stem cell (hiPSC)-derived liver and islet organoids were 30-day 3D co-cultured. It was able to recapitulate liver-islet axis activity in normal and type 2 diabetes conditions and most importantly, the system is available to monitor drug response[0]. Likewise, further interactive axes and systems of this kind will emerge in the future in organoid simulation studies and progressively become the main in vitro models. Depending on all the above-stated technological development, the use of organoids as far as the research of individualized metabolisms is concerned will be more comprehensive and clear. Metabolic diseased organoids derived in patients are capable of retaining the unique genetic background and pathological characteristics, which can be applied to investigate the mechanisms of interaction between genes and the environment. In addition to the technology of gene editing, organicoid models with certain pathogenic mutations may be built to decipher genome pathways of illness presence and located intervented targets to short cut precise examination of single diseases. Further, the effects of drugs may be reflected in organoids, which will enable the clinicians to determine the effectiveness and cure rates of various drugs on patients accurately. Organoids are also research models as well as highly promising as transplantation substitutes. In mice suffering liver damage the human hepatocyte organoids (HGOs) which maintained full metabolic activity upon introduction into the host actually engrafted, restored liver lobule architecture, and extended the lifespan of the model organisms dramatically[0]. Even though this is still some distance off the clinical human transplantation, this is a new ray of hope to cell therapy in terminal metabolic liver disease among other diseases. Nevertheless, the standardization and industrialization cannot be separated with the enormous promotion and utilization of technology. China, the United States, the European Union and other nations have then passed the suitable legal notices and are slowly developing controls on the organoid research[0]. This suggests that the organoid study is becoming popular and encouraged by governments. Further, organoid studies are in their infantile developmental phase and there is so much to be ventured into. The research on individualized metabolism offers a vast amount of research participants and a massive market of organoid research. Organoid models of research on individuals are opening up uncharted avenues of development.

6. Conclusion

Organoid technology, as a powerful in vitro model connecting genotype and phenotype, is profoundly changing the standard paradigm of individualized metabolism research. This is a systematic review providing an overview of the entire environment of this area, including theoretical basis and implementation opportunities. The fundamental advantage of organoid models is that they globally simulate the three-dimensional architecture, cellular heterogeneity, and the essential functions of donor tissues, as well as to a maximum, retain the genetic and phenotypic traits of the donor subjects, and thus are the best organoid models to study metabolic heterogeneity. They can be widely applied, such as the study of metabolic reprogramming, response to chemotherapy and targeted drugs, and immunotherapy efficacy, further encouraging the study of disease mechanisms and new targeted therapies. The development of the research organoids has been largely dependent on the development and incorporation of analytic technologies such as the metabolomics, proteomics and imaging of high resolution. Artificial intelligence further streamlines (the organisational preparation of an organoid culture, data processing, and prediction of effectiveness) leading research to the field of intelligence and automation.

Nevertheless, the extensive use of the technology is still facing significant challenges: a lack of biomimicry regarding self-vascularization, innervation, and implementation of immune

components; the problem with genetic and functional stability over time culture; limitations in sensitivity and complexity of the interpretation of the data to detect metabolic processes; and a more serious problem associated with the absence of universal culture, detection, and analysis protocols on a global scale. Also, a significant barrier to the laboratory-to-clinical translation and regulatory pathway has been identified: its high cost and ambiguity in clinical translation and regulatory pathways. Individualized research on metabolism using organoids will bring breakthroughs in multiple dimensions in the future: a positive change in the policy and regulatory environment is creating an opening; the advancement of vascularization and multi-organ-on-a-chips will considerably increase the systematicity and physiological relevance of models; and the integration of AI and multi-omics will also allow virtual screening and accurate prediction. Eventually, through developing extensive standardization frameworks and through the encouragement of automated, mass-scale production, organoid technology is set to become a luxury of research equipment in small-scale clinical treatment and diagnosis as a routine. It has a prospect of offering new avenues to overcome complicated metabolic illness such as cancer diabetes and fatty liver disease as a crucial key to the precision medicine.

Reference：

Gilbert PM, Hofmann S, Ng HH, Vankelecom H, Wells JM. Organoids in endocrine and metabolic research: current and emerging applications. Nat Rev Endocrinol. 2024 Apr;20(4):195-201. doi: 10.1038/s41574-023-00933-1. Epub 2024 Jan 5. PMID: 38182746.

Verstegen MMA, Coppes RP, Beghin A, De Coppi P, Gerli MFM, de Graeff N, Pan Q, Saito Y, Shi S, Zadpoor AA, van der Laan LJW. Clinical applications of human organoids. Nat Med. 2025 Feb;31(2):409-421. doi: 10.1038/s41591-024-03489-3. Epub 2025 Feb 3. PMID: 39901045.

Sato T, Vries RG, Snippert HJ, van de Wetering M, Barker N, Stange DE, van Es JH, Abo A, Kujala P, Peters PJ, Clevers H. Single Lgr5 stem cells build crypt-villus structures in vitro without a mesenchymal niche. Nature. 2009 May 14;459(7244):262-5. doi: 10.1038/nature07935. Epub 2009 Mar 29. PMID: 19329995.

Lin L, DeMartino J, Wang D, van Son GJF, van der Linden R, Begthel H, Korving J, Andersson-Rolf A, van den Brink S, Lopez-Iglesias C, van de Wetering WJ, Balwierz A, Margaritis T, van de Wetering M, Peters PJ, Drost J, van Es JH, Clevers H. Unbiased transcription factor CRISPR screen identifies ZNF800 as master repressor of enteroendocrine differentiation. Science. 2023 Oct 27;382(6669):451-458. doi: 10.1126/science.adi2246. Epub 2023 Oct 26. PMID: 37883554.

Velasco S, Kedaigle AJ, Simmons SK, Nash A, Rocha M, Quadrato G, Paulsen B, Nguyen L, Adiconis X, Regev A, Levin JZ, Arlotta P. Individual brain organoids reproducibly form cell diversity of the human cerebral cortex. Nature. 2019 Jun;570(7762):523-527. doi: 10.1038/s41586-019-1289-x. Epub 2019 Jun 5. PMID: 31168097; PMCID: PMC6906116.

Xiang C,Cai HW.Research progress of cardiovascular organoid models[J/OL].Chinese Journal of Comparative Medicine,1-10[2026-03-03].https://link.cnki.net/urlid/11.4822.R.20260210.1650.004.

Yu HX,Wang L,Cai PY.Recent advances in development and application of organoids in dermatology[J].Journal of Clinical Dermatology,2026,55(02):145-148.DOI:10.16761/j.cnki.1000-4963.2026.02.017.

Yang J, Song SL, Castro-Perez J, Plumb RS, Xu GW. [Metabonomics and its applications]. Sheng Wu Gong Cheng Xue Bao. 2005 Jan;21(1):1-5. Chinese. PMID: 15859320.

Chang Y, Zhang W, Chen K, Wang Z, Xia S, Li H. Metabonomics window into plateau hypoxia. J

Int Med Res. 2019 Nov;47(11):5441-5452. doi: 10.1177/0300060519879323. Epub 2019 Oct 9. PMID: 31594434; PMCID: PMC6862876.

Bujak R, Struck-Lewicka W, Markuszewski MJ, Kaliszan R. Metabolomics for laboratory diagnostics. J Pharm Biomed Anal. 2015 Sep 10;113:108-20. doi: 10.1016/j.jpba.2014.12.017. Epub 2014 Dec 25. PMID: 25577715.

Klupczyńska A, Dereziński P, Kokot ZJ. METABOLOMICS IN MEDICAL SCIENCES--TRENDS, CHALLENGES AND PERSPECTIVES. Acta Pol Pharm. 2015 Jul-Aug;72(4):629-41. PMID: 26647618.

Liu J,Pan HY,Zhang HP.Expert Consensus on the Application of Metabolomics in Precision Health Management[J].Journal of Health Examination and Management,2023,4(01):3-10.

You J, Cui XH, Chen YL, Wang YX, Li HY, Qiang YX, Cheng JY, Deng YT, Guo Y, Ren P, Zhang Y, He Y, He XY, Chen SD, Zhang YR, Huang YY, Mao Y, Feng JF, Cheng W, Yu JT. Mapping the plasma metabolome to human health and disease in 274,241 adults. Nat Metab. 2025 Nov;7(11):2366-2384. doi: 10.1038/s42255-025-01371-1. Epub 2025 Sep 19. PMID: 40973818; PMCID: PMC12638258.

Qiang YX, Wang YX, He XY, Deng YT, Ge YJ, Wu BS, Jia Y, Feng JF, Cheng W, Yu JT. Genetic architecture of plasma metabolome in 254,825 individuals. Nat Commun. 2025 Sep 19;16(1):8272. doi: 10.1038/s41467-025-62126-w. PMID: 40973927; PMCID: PMC12449471.

Bhinderwala F, Powers R. NMR Metabolomics Protocols for Drug Discovery. Methods Mol Biol. 2019;2037:265-311. doi: 10.1007/978-1-4939-9690-2_16. PMID: 31463851; PMCID: PMC7025395.

Mussap M, Loddo C, Fanni C, Fanos V. Metabolomics in pharmacology - a delve into the novel field of pharmacometabolomics. Expert Rev Clin Pharmacol. 2020 Feb;13(2):115-134. doi: 10.1080/17512433.2020.1713750. Epub 2020 Jan 20. PMID: 31958027.

Huang Y, Li J, Song S, Du B, Cao Y, Wang Y, Fu H, Zhou T, Yu S, Liu Y, Wang K, Cao Z, Guo X, Xie C, Xie Q. Blood metabolic panels for identifying significant fibrosis and inflammation in patients with MASLD. Cell Rep Med. 2026 Jan 20;7(1):102522. doi: 10.1016/j.xcrm.2025.102522. Epub 2025 Dec 19. PMID: 41421352; PMCID: PMC12866143.

Jiang X, Zhu F, Graça G, Du X, Ran J, Ahmadizar F, Wood AC, Zhou Y, Scholtens DM, Farzaneh A, Ikram MA, Kuang A, le Roux CW, Gadgil MD, Cornelis MC, Taylor KD, Guo X, Ghanbari M, Rasmussen-Torvik LJ, Tracy RP, Bertoni AG, Rotter JI, Herrington DM, Greenland P, Kavousi M, Zhong VW. Serum Metabolomic Profiling of Incident Type 2 Diabetes Mellitus in the Multi-ethnic Study of Atherosclerosis and Rotterdam Study. J Clin Endocrinol Metab. 2025 Jul 15;110(8):e2700-e2710. doi: 10.1210/clinem/dgae812. PMID: 39566105; PMCID: PMC12261090.

Wang H, Wang L, Zhu X, He M, Zhong L, Lv Y, Li Q, Jiang Q, Zhang C, Liu X, Zou D. Patient-derived organoids predict responses to chemotherapy and PARP inhibitors in advanced ovarian cancer. J Transl Med. 2026 Jan 6;24(1):55. doi: 10.1186/s12967-025-07112-y. PMID: 41491716; PMCID: PMC12797791.

He Y, Gao M, Zhu X, Peng W, Zhou Y, Cheng J, Bai L, Bao J. Large-Scale Formation and Long-Term Culture of Hepatocyte Organoids From Streamlined In Vivo Genome-Edited GGTA1-/- Pigs for Bioartificial Liver Applications. Xenotransplantation. 2024 Jul-Aug;31(4):e12878. doi: 10.1111/xen.12878. PMID: 39166823.

Rao J, Song C, Hao Y, Chen Z, Feng S, Xu S, Wu X, Xuan Z, Fan Y, Li W, Li J, Ren Y, Li J, Cheng

F, Gu Z. Leveraging Patient-Derived Organoids for Personalized Liver Cancer Treatment. Int J Biol Sci. 2024 Oct 7;20(13):5363-5374. doi: 10.7150/ijbs.96317. PMID: 39430248; PMCID: PMC11488587.

Zhao Y, Li S, Zhu L, Huang M, Xie Y, Song X, Chen Z, Lau HC, Sung JJ, Xu L, Yu J, Li X. Personalized drug screening using patient-derived organoid and its clinical relevance in gastric cancer. Cell Rep Med. 2024 Jul 16;5(7):101627. doi: 10.1016/j.xcrm.2024.101627. Epub 2024 Jul 3. PMID: 38964315; PMCID: PMC11293329.

Kim Y, Kang M, Mamo MG, Adisasmita M, Huch M, Choi D. Liver organoids: Current advances and future applications for hepatology. Clin Mol Hepatol. 2025 Feb;31(Suppl):S327-S348. doi: 10.3350/cmh.2024.1040. Epub 2024 Dec 26. PMID: 39722609; PMCID: PMC11925438.

Wang ZC,Zhao YH,Yuan KX.The Application of Organoid Technology in the Research of Central Nervous System Tumors [J].Medical Journal of Peking Union Medical College Hospital,2025,16(04):836-846.

Xu H, Jiao D, Liu A, Wu K. Tumor organoids: applications in cancer modeling and potentials in precision medicine. J Hematol Oncol. 2022 May 12;15(1):58. doi: 10.1186/s13045-022-01278-4. PMID: 35551634; PMCID: PMC9103066.

Zhang A, Sun H, Wang P, Han Y, Wang X. Recent and potential developments of biofluid analyses in metabolomics. J Proteomics. 2012 Feb 2;75(4):1079-88. doi: 10.1016/j.jprot.2011.10.027. Epub 2011 Nov 4. PMID: 22079244.

Kømurcu KS, Zawadzka ME, Meszka I, Aizenshtadt A, Hrušková H, Aakervik LE, Thorne JL, Wilson SR, Krauss SJK, Røberg-Larsen H. A Validated Mass Spectrometry Platform for Oxysterol Analysis of Single Human Gastruloids and Liver Organoids. Anal Chem. 2026 Feb 23. doi: 10.1021/acs.analchem.5c07140. Epub ahead of print. PMID: 41731721.

Hu T, Shukla SK, Vernucci E, He C, Wang D, King RJ, Jha K, Siddhanta K, Mullen NJ, Attri KS, Murthy D, Chaika NV, Thakur R, Mulder SE, Pacheco CG, Fu X, High RR, Yu F, Lazenby A, Steegborn C, Lan P, Mehla K, Rotili D, Chaudhary S, Valente S, Tafani M, Mai A, Auwerx J, Verdin E, Tuveson D, Singh PK. Metabolic Rewiring by Loss of Sirt5 Promotes Kras-Induced Pancreatic Cancer Progression. Gastroenterology. 2021 Nov;161(5):1584-1600. doi: 10.1053/j.gastro.2021.06.045. Epub 2021 Jul 8. PMID: 34245764; PMCID: PMC8546779.

Yoshida GJ. Applications of patient-derived tumor xenograft models and tumor organoids. J Hematol Oncol. 2020 Jan 7;13(1):4. doi: 10.1186/s13045-019-0829-z. PMID: 31910904; PMCID: PMC6947974.

Xu H, Jiao D, Liu A, Wu K. Tumor organoids: applications in cancer modeling and potentials in precision medicine. J Hematol Oncol. 2022 May 12;15(1):58. doi: 10.1186/s13045-022-01278-4. PMID: 35551634; PMCID: PMC9103066.

Dao V, Yuki K, Lo YH, Nakano M, Kuo CJ. Immune organoids: from tumor modeling to precision oncology. Trends Cancer. 2022 Oct;8(10):870-880. doi: 10.1016/j.trecan.2022.06.001. Epub 2022 Jun 27. PMID: 35773148; PMCID: PMC9704769.

Igarashi R, Oda M, Okada R, Yano T, Takahashi S, Pastuhov S, Matano M, Masuda N, Togasaki K, Ohta Y, Sato S, Hishiki T, Suematsu M, Itoh M, Fujii M, Sato T. Generation of human adult hepatocyte organoids with metabolic functions. Nature. 2025 May;641(8065):1248-1257. doi: 10.1038/s41586-025-08861-y. Epub 2025 Apr 16. PMID: 40240606.

Wang D, Villenave R, Stokar-Regenscheit N, Clevers H. Human organoids as 3D in vitro platforms for drug discovery: opportunities and challenges. Nat Rev Drug Discov. 2025 Nov 12. doi:

10.1038/s41573-025-01317-y. Epub ahead of print. PMID: 41225057.
Ojo BA, Zhu Y, Heo L, Fox SR, Qiao Y, Waddell A, Moreno-Fernandez ME, Gibson M, Tran T, Dunn AL, Elknawy EIA, Saini N, López-Rivera JA, Divanovic S, Dai Y, de Jesus Perez VA, Rosen MJ. Patient-derived colon epithelial organoids reveal lipid-related metabolic dysfunction in pediatric ulcerative colitis. Nat Commun. 2025 Dec 10;16(1):11026. doi: 10.1038/s41467-025-65988-2. PMID: 41372139; PMCID: PMC12695892.
Xiang D, He A, Zhou R, Wang Y, Xiao X, Gong T, Kang W, Lin X, Wang X; PDO-based DST Consortium; Liu L, Chen YG, Gao S, Liu Y. Building consensus on the application of organoid-based drug sensitivity testing in cancer precision medicine and drug development. Theranostics. 2024 May 27;14(8):3300-3316. doi: 10.7150/thno.96027. PMID: 38855182; PMCID: PMC11155402.
Neal JT, Li X, Zhu J, Giangarra V, Grzeskowiak CL, Ju J, Liu IH, Chiou SH, Salahudeen AA, Smith AR, Deutsch BC, Liao L, Zemek AJ, Zhao F, Karlsson K, Schultz LM, Metzner TJ, Nadauld LD, Tseng YY, Alkhairy S, Oh C, Keskula P, Mendoza-Villanueva D, De La Vega FM, Kunz PL, Liao JC, Leppert JT, Sunwoo JB, Sabatti C, Boehm JS, Hahn WC, Zheng GXY, Davis MM, Kuo CJ. Organoid Modeling of the Tumor Immune Microenvironment. Cell. 2018 Dec 13;175(7):1972-1988.e16. doi: 10.1016/j.cell.2018.11.021. PMID: 30550791; PMCID: PMC6656687.
Liu H, Wang R, Li X, Wu Z, Sun J, Lu W, Wang X. [Advances in organoids of the digestive system]. Sheng Wu Gong Cheng Xue Bao. 2023 Apr 25;39(4):1332-1350. Chinese. doi: 10.13345/j.cjb.220549. PMID: 37154309.
Muthubharathi BC, Gowripriya T, Balamurugan K. Metabolomics: small molecules that matter more. Mol Omics. 2021 Apr 1;17(2):210-229. doi: 10.1039/d0mo00176g. Epub 2021 Feb 18. PMID: 33598670.
Jin, Y, Park, S, Cho, S. Organoid analytical toolkits NAT REV BIOENG. 2026; doi: 10.1038/s44222-025-00384-5
Yang R, Qi Y, Zhang X, Gao H, Yu Y. Living biobank: Standardization of organoid construction and challenges. Chin Med J (Engl). 2024 Dec 20;137(24):3050-3060. doi: 10.1097/CM9.0000000000003414. Epub 2024 Dec 12. PMID: 39663560; PMCID: PMC11706585.
Ahn SJ, Lee S, Kwon D, Oh S, Park C, Jeon S, Lee JH, Kim TS, Oh IU. Essential Guidelines for Manufacturing and Application of Organoids. Int J Stem Cells. 2024 May 30;17(2):102-112. doi: 10.15283/ijsc24047. Epub 2024 May 20. PMID: 38764240; PMCID: PMC11170116.
National Medical Products Administration Center for Drug Evaluation. Notice of the National Medical Products Administration Center for Drug Evaluation on the Release of the Technical Guidance Principles for Model-Guided Rare Disease Drug Development: 2025 No. 25[EB/OL]. (2025-07-30)[2026-03-04]. https://www.cde.org.cn/main/news/viewinfoCommon/6af9e335e63bbcfc762a3d191ff8b719
U.S. Congress. FDA Modernization Act 3.0 (S. 5046)[EB/OL]. (2024-12-13)[2026-03-04]. https://www.govinfo.gov/app/details/BILLS-118s5046.
International Society of Organoid Research (ISoOR). ISoOR-International Standards for Organoid Biobanking (ISoOR-ISOB): 1st Edition[EB/OL]. (2025-11-03)[2026-03-04]. https://www.isoor.org/official-release-of-isoor-isob.html
Bai L, Su J. Artificial Intelligence Virtual Organoids (AIVOs). Bioact Mater. 2025 Dec 22;59:45-

68. doi: 10.1016/j.bioactmat.2025.12.030. PMID: 41536916; PMCID: PMC12796111.
Tan S, Ding Y, Wang W, Rao J, Cheng F, Zhang Q, Xu T, Hu T, Hu Q, Ye Z, Yan X, Wang X, Li M, Xie P, Chen Z, Liang G, Pu Y, Zhang J, Gu Z. Development of an AI model for DILI-level prediction using liver organoid brightfield images. Commun Biol. 2025 Jun 7;8(1):886. doi: 10.1038/s42003-025-08205-6. PMID: 40483291; PMCID: PMC12145446.
Miao Y, Pek NM, Tan C, Jiang C, Yu Z, Iwasawa K, Shi M, Kechele DO, Sundaram N, Pastrana-Gomez V, Sinner DI, Liu X, Lin KC, Na CL, Kishimoto K, Yang MC, Maharjan S, Tchieu J, Whitsett JA, Zhang YS, McCracken KW, Rottier RJ, Kotton DN, Helmrath MA, Wells JM, Takebe T, Zorn AM, Chen YW, Guo M, Gu M. Co-development of mesoderm and endoderm enables organotypic vascularization in lung and gut organoids. Cell. 2025 Aug 7;188(16):4295-4313.e27. doi: 10.1016/j.cell.2025.05.041. Epub 2025 Jun 30. PMID: 40592324.
Abilez OJ, Yang H, Guan Y, Shen M, Yildirim Z, Zhuge Y, Venkateshappa R, Zhao SR, Gomez AH, El-Mokahal M, Dunkenberger L, Ono Y, Shibata M, Nwokoye PN, Tian L, Wilson KD, Lyall EH, Jia F, Wo HT, Zhou G, Aldana B, Karakikes I, Obal D, Peltz G, Zarins CK, Wu JC. Gastruloids enable modeling of the earliest stages of human cardiac and hepatic vascularization. Science. 2025 Jun 5;388(6751):eadu9375. doi: 10.1126/science.adu9375. Epub 2025 Jun 5. PMID: 40472086; PMCID: PMC12815606.
Tao T, Deng P, Wang Y, Zhang X, Guo Y, Chen W, Qin J. Microengineered Multi-Organoid System from hiPSCs to Recapitulate Human Liver-Islet Axis in Normal and Type 2 Diabetes. Adv Sci (Weinh). 2022 Feb;9(5):e2103495. doi: 10.1002/advs.202103495. Epub 2021 Dec 23. PMID: 34951149; PMCID: PMC8844474.