China Microbiome Initiative: Opportunities and Challenges Postprint

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Abstract

The microbiome refers to all microorganisms and their genetic information within a specific environment or ecosystem, including their cellular populations and quantities, and all genetic material (genomes). It defines the entirety encompassing microbial communities and their complete genetic and physiological functions, with its connotation including the interactions between microorganisms and their environment and hosts. Microbiomics is an emerging discipline, and achievements from microbiome research will undoubtedly provide a continuous source of innovative vitality for national economic and social development and the improvement of human quality of life. Therefore, microbiomics is also a strategic scientific and technological field that countries worldwide are competing to develop; developed nations such as the United States and Japan have already deployed national plans to support microbiome research. Based on analyzing the domestic development status and integrating the national needs during China' s development process, this article analyzes the opportunities and challenges facing China' s microbiome research and proposes the fundamental principles for deploying the China Microbiome Initiative: "national needs-oriented, scientific hypothesis-driven, and technological innovation-supported." It recommends establishing the China Microbiome Initiative as a national key research and development program; it explores the key fields and content of the China Microbiome Initiative, involving areas such as health, environment, industry and agriculture, and marine science. It is hoped that through the implementation of the China Microbiome Initiative, China will lead international large-scale scientific programs and strengthen its discourse power in relevant fields, significantly enhance its capacity for scientific and technological innovation and the transformation of scientific achievements, foster a batch of strategic emerging industries based on disruptive technologies, and make due contributions to China' s economic and social development and the progress of human civilization.

Full Text

Preamble

On May 13, 2016, the United States announced the launch of its National Microbiome Initiative, focusing global scientific and governmental attention on microbiome research as a strategic frontier in worldwide technological development. Document No. 1 [2017] from the Party Leadership Group of China' s Ministry of Science and Technology called for deepening implementation of the innovation-driven development strategy, strengthening foundational frontier research, enhancing original innovation capabilities, and developing major disruptive technologies. In domains including microbiome, artificial intelligence, and deep earth exploration, the document advocated innovating organizational models and management mechanisms to deploy several major initiatives. To further advance China' s microbiome initiative and gradually gain greater voice in international microbiome programs, this journal publishes this special issue on "China Microbiome Initiative," guided by Academician Zhao Guoping from Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, and Researcher Liu Shuangjiang from Institute of Microbiology, Chinese Academy of Sciences.

China Microbiome Initiative: Opportunities and Challenges

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Abstract

Microbiome refers to the totality of microorganisms and their collective genetic information within a specific environment or ecosystem, including their cellular populations and quantities, and all genetic material (genomes). It encompasses microbial communities and their complete genetic and physiological functions, including interactions between microorganisms and their environment and hosts. Microbiomics is an emerging frontier discipline. The achievements from microbiome research will provide continuous innovative vitality for national economic and social development and for improving human quality of life. Consequently, microbiomics has become a strategic technological field contested by nations worldwide, with developed countries such as the United States and Japan having already deployed national plans to support microbiome research.

Based on analysis of domestic development status and in conjunction with national needs during China' s development, this article analyzes the opportunities and challenges facing microbiome research in China. It proposes the fundamental principles of "national demand orientation, scientific hypothesis-driven, and technological innovation support" for deploying the China Microbiome Initiative. The article recommends establishing a national key research and development program for the China Microbiome Initiative and discusses its priority areas and content, covering health, environment, industry and agriculture, and marine domains. Through implementation of the China Microbiome Initiative, it is hoped that China can lead international large-scale scientific programs, strengthen its discourse power in relevant fields, significantly enhance its scientific innovation and technology transformation capabilities, spawn a batch of strategic emerging industries based on disruptive technologies, and make due contributions to China' s economic and social development and human civilization progress.

Keywords: China Microbiome Initiative, microbiomics, science and technology, strategic and planning proposal

1. From Microorganisms to Microbiome

Among all existing life forms on Earth, microorganisms emerged earliest approximately 3.5 billion years ago, exhibiting the most extensive distribution, largest biomass, and richest biodiversity. The first important characteristic of microorganisms is their "micro" scale—their physical dimensions fall below human visual resolution, making most individual microorganisms invisible to the naked eye. Overcoming this "micro" limitation to understand microorganisms represented the first condition for microbiology' s birth, with microscopy technology providing the essential technical support. However, microscopy only enabled observation; the second technical breakthrough that catalyzed microbiology' s formation was microbial cultivation technology [1,2]. The essence of this breakthrough involved transforming microorganisms from single-cell to multicellular population states by creating specific environmental conditions, enabling investigation of physiological, biochemical, genetic, metabolic, and pathogenic properties. The cultivation process itself revealed another crucial biological characteristic of microorganisms: their intimate interaction with the environment. This interaction manifests first in the extensive distribution and diversity of microorganisms (far exceeding that of multicellular "higher organisms") and their vital roles throughout the biosphere.

For over a century, scientists could culture and study only a tiny fraction of all microorganisms in nature due to limitations in cultivation methods and techniques. This led to the concept of "uncultured microorganisms," which constitute the vast majority of natural microbes (for example, activated sludge in wastewater treatment—used for over a hundred years—is primarily microbial, with unknown microorganisms accounting for over 85%; 99% of marine and terrestrial microorganisms remain currently unculturable) [3]. For years, many have compared uncultured microorganisms to dark matter in the universe to inspire exploration of this unimaginable microbial world, thereby driving development of microbial cultivation technology, single-cell/single-molecule technology, high-throughput technology, microfluidics, culture-independent technology, imaging technology, and sequencing technology.

However, breakthroughs in understanding the biological characteristics and functions of "uncultured microorganisms" (at both single-cell/pure culture and multicellular/multispecies population + environmental interaction levels), particularly the molecular mechanisms and their integration across multiple spatiotemporal scales (systems biology mechanisms), depended on a third technological breakthrough: the widespread application of metagenomics technology. This directly enabled two advances: first, microbial discovery and characterization could transcend cellular and biochemical frameworks to reach the genetic/genomic level, typically manifested in the complete genome determination of an "uncultured" microorganism. Second, understanding microbial functions could move beyond "pure culture" limitations to the microbial community level, even integrating community metagenomes with environmental genomes for study. Both advances point to a crucial conceptual leap in microbiology' s history: the "microbiome."

Microbiome refers to all microorganisms and their genetic information in a specific environment or ecosystem, including cellular populations and quantities, and all genetic material (genomes). It encompasses microbial communities and their complete genetic and physiological functions, including interactions with environments and hosts. Microbiomics takes the microbiome as its object, studying its structure and function, inter-population relationships and mechanisms, interactions with environments or hosts, and ultimately regulating microbial community growth and metabolism to serve human health and sustainable social development.

2. Significance of Microbiome Research

2.1 Microbiome as a Strategic Frontier in the New Round of Scientific Revolution

From a scientific perspective, revealing the operational mechanisms of life and various ecosystem levels in Earth' s biosphere has reached a point where understanding microbial community mechanisms is essential. From a technology-driven perspective, initiatives such as the Human Microbiome Project and Earth Microbiome Project have essentially achieved transformation from core technology development to critical knowledge leaps, demonstrating the enormous potential of both "Top-Down" systems biology and "Bottom-Up" synthetic biology approaches for studying complex biological systems like microbiomes. From an application perspective, comprehensively and systematically analyzing microbiome structure and function and clarifying relevant regulatory mechanisms will bring revolutionary new ideas for solving major systemic problems facing human society in health, agriculture, and environment. Microbiological technology innovations will further provide disruptive technical means and unusual solutions. Such an innovation chain and service chain—from basic research and translational research to technology innovation and industrial application—is rapidly forming and expanding into industry, agriculture, medicine, and environment.

2.2 International Microbiome Research at a Turning Point with Major Opportunities

Based on preliminary breakthroughs both domestically and internationally, microbiome research has become a strategic "high ground" in the new round of international scientific revolution, with substantial resource investment from governments and societies in Western developed countries and increasing numbers of researchers and institutions involved [4]. Through this rapid development, the need for new multidisciplinary and internationally collaborative large-scale scientific program organizational models has become more recognized. Consequently, scientists from China, the United States, Germany, and other countries published articles in *Nature* calling for an "International Microbiome Initiative" [5]. Four major trends deserve attention regarding the proposal of microbiome and international scientific competition.

2.2.1 Expanding Research Scope with Clearer Application Orientation The focus has shifted from previous microbial resource surveys and microbiome applications in energy and health to comprehensive consideration of health, agriculture, environment, and other directions. The United States previously deployed the "Genomes to Life Program" (launched 2002), "Human Microbiome Project" (launched 2008, total investment $170 million), and "Earth Microbiome Project" (launched 2010); Japan had the "Human Metagenome Research Project" (launched 2005); Canada had the "Microbiome Research Initiative" (launched 2007); and the EU had the "Human Intestinal Metagenome Project" (launched 2008), all focusing on microbial resource surveys and microbiome applications in energy and health. The new "Unified Microbiome Initiative" proposed by the United States in 2015 (with at least $400 million annually, potentially rising to $500-600 million annually within 2-5 years) emphasizes the need to simultaneously address microbiome application potential in health, agriculture, environment, and ecology.

2.2.2 Emphasis on Technology Development and Interdisciplinary Convergence The focus of technological development has shifted from traditional microbiological techniques to new-generation microbiological technologies represented by culturomics, high-throughput sequencing, imaging technology, and bioinformatics technology. Emphasis is placed on innovation in sampling (in situ, non-invasive, breaking unculturable barriers), detection (quantitative/real-time, "omics" technologies, single-cell/high-throughput), statistics (research design/ecological guidance, bioinformatics + big data analysis), and validation (model systems + synthetic biology technology) to drive in-depth microbiome development, which increasingly requires multidisciplinary convergence.

2.2.3 Innovation in Research Organization Mechanisms Based on the four major characteristics of microbiome research— "broad involvement, complex and intensive data, enabling technology engineering, and interdisciplinary convergence" —the demand for project organization mechanism innovation is more urgent. Microbiome science research and technology development project organization needs to shift from exploratory basic research to goal-oriented systematic data collection and mechanism research and integrated research and development mechanisms, effectively solving standardization issues in sample and metadata collection, data integration analysis mechanisms and technical problems, and mechanisms and engineering technology issues in translating basic research to translational research and industrial applications. Additionally, attention must be paid to cooperation and resource and data integration in microbiome research and applications across different ecosystems to truly achieve interdisciplinary and cross-field collaborative research.

2.2.4 Large-Scale Scientific Programs and Global Cooperation The urgent dependence on large-scale scientific programs and global cooperation provides new opportunities for latecomer countries to catch up with early initiators like the United States and lead international cooperation. Large-scale scientific programs and global cooperation can more effectively promote research standardization and coordination, discovering universal patterns affecting the globe by integrating and correlating data from thousands of individual laboratories. Previously, the United States dominated international large-scale biotechnology programs with its advantages in biotechnology. With the launch of the U.S. "Unified Microbiome Initiative," the EU, China, Brazil, France, Japan, and other countries and regions will also launch their own microbiome initiatives to compete. Latecomer countries, relying on resource characteristics and advantages in technology route introduction, integration, and innovation, combined with strong demand in certain fields, can adopt "asymmetric" strategies to achieve corner overtaking in specific domains, solve national economic and livelihood needs, and lead international cooperation.

3. Major Breakthroughs in Microbiome Research

Since the microbiome concept was proposed, interest has continuously increased. A Baidu search for "microbiome" yields over 6 million results, and research reports and publications show exponential growth (Figure 1 [Figure 1: see original paper]). Analysis of significant achievements across various fields reveals that human health microbiome receives the greatest attention. In particular, gastrointestinal microbiome research has discovered correlations between gut microbiome and diabetes, liver disease, obesity, and mental illness [6,7]. Fecal microbiota transplantation for treating *Clostridium difficile*-induced dysentery not only revolutionized traditional treatment approaches but also further proposed the new concept that gastrointestinal microbiome balance critically impacts physical health [8]. Current research has found that the human gut harbors up to 1,000 microbial species, with individuals averaging 160 microbial species, and microbial cell numbers are ten times those of human cells. These microorganisms are closely related to human aging and traditional Chinese medicine efficacy [9,10].

The Earth Microbiome Project (EMP), launched in 2010 in the United States, plans to collect 200,000 samples globally to comprehensively and systematically gather data on microbial populations, quantities, distribution, structure, and function in Earth' s ecosystems, including natural environments (land, ocean, soil, water bodies, etc.) and artificial environments (such as wastewater treatment bioreactors). This ambitious plan was once criticized as impossible, but by 2014, the project had completed sequencing and analysis of 30,000 samples, greatly increasing confidence in its realization [11]. Through EMP implementation, unified and continuously improving research methods have been established, completing microbiome data collection and analysis in environments such as Midwest U.S. prairie soils, Siberian permafrost, and Gulf of Mexico deep-sea sediments. These efforts have revealed microbial characteristics in these environments, regulatory mechanisms driving microbial community evolution, organic matter transformation, and responses to environmental changes, and discovered that human activities may exert enormous impacts on microbial ecosystems—a finding increasingly recognized and widely concerned by scientists [12].

4. Foundation and Challenges for Microbiome Research Development in China

China possesses three major advantages for developing microbiome research but also faces two major challenges in technology and organizational management.

4.1 Advantage 1: Rich Environmental and Biological Resources with Integrated Platforms

China possesses abundant environmental and biological resources, with diverse environmental resources harboring microbiomes of unlimited application potential. China' s population genetic diversity, combined with various regional diets and lifestyles, determines that China has numerous distinct and characteristic human microbiomes. China has a wide variety of agricultural, forestry, and livestock species growing in diverse environments, plus unique animal and plant resources (such as characteristic medicinal plants and unique wildlife like giant pandas). Microbiome resources in this area are not only abundant but also distinctive, becoming important resources for further development. China has a long history and massive fermentation industry, with a considerable portion being complex microbial community fermentation, naturally making it an important object of microbiome research. China also faces heavy tasks in environmental protection and restoration of polluted ecological systems, posing urgent demands and missions for microbiome research.

4.2 Advantage 2: Long-Term State Funding with High-Level Talent and Foundational Achievements

In terms of scientific research funding, support from the National Natural Science Foundation of China has gradually increased, supplemented by the "973" Program, "863" Program, and the Chinese Academy of Sciences' Strategic Priority Research Program. Currently, annual research and development funding in China' s microbiology field approaches 400 million RMB. China has established a solid foundation in microbiology, microbial ecology, microbial genomics, and functional genomics, particularly in microbial species resources, classification and evolution, physiology and metabolism, genetics and development, and impacts on environments and hosts. Substantial progress has been made in soil microbiology and agriculture, with some achievements reaching international parallel or even leading positions. For example, China participated in the Human Microbiome Project and proposed new concepts such as targeting gut microbiota for chronic disease prevention, cultivating a group of high-level research teams. Driven by these rich resources and strong demands, China' s microbiome research launch has been basically synchronized with international efforts. Benefiting from domestic superior genomics and other omics platform services, research standards have essentially reached the international frontier. However, similar to common problems in China' s life sciences research, deficiencies in this field can be summarized in three aspects: (1) relatively narrow research coverage; (2) few original works in analysis, experimental verification, and application development; and (3) establishment of systematic research systems still awaits development.

4.3 Advantage 3: Institutionalized Research Systems Such as State Key Laboratories Oriented Toward Basic and Applied Research, with Consistent Emphasis on Interdisciplinary Integration Between Microbiology and Other Disciplines

In microbiology basic and applied basic research and microbiology technology development and application transformation, China has established eight State Key Laboratories and specialized research institutes oriented toward general, agricultural, industrial, environmental, and medical microbiology research. This institutionalized research system supports the growth of microbiology research teams and long-term, stable investigation, collection, preservation, and identification of microbial resources and technology development. China's microbiology community has long emphasized interdisciplinary integration between microbiology and various disciplines, promoting microbiology' s active role in both basic research and application development. Guided by this strategic thinking, these microbiology research institutions have long maintained exchange and cooperation with other research institutions in corresponding fields, ensuring microbiology research integrates with various "environmental" studies and plays a role in development applications.

4.4 Challenge: Organizational Management Innovation and Breaking Technology Bottlenecks

Given the above foundations and advantages for conducting microbiome research in China, why hasn' t overall development reached internationally first-class levels? The core issue remains the lack of overall systematic design, urgently needing to grasp key scientific questions and break through technology bottlenecks. Specifically, in project organization and management, "joint operations" across fields and departments targeting major problems have not been realized. In terms of resources and data, true sharing has not been achieved. In research methodology and technology innovation, interdisciplinary integration is insufficient, particularly lacking convergence with mathematics, computational science, and physics. Big data processing and analysis technologies are deficient, and talent in these areas is lacking. These issues are interrelated and require comprehensive consideration and integrated solutions.

5. Considerations and Recommendations for the China Microbiome Initiative

5.1 Overall Planning Framework

As previously described, microbiome research faces an unprecedented period of opportunity and window. The opportunity lies in clear basic development directions and research methods, with conditions for scientific and technological application breakthroughs basically mature. Combined with China' s foundation and advantages in this direction and favorable international cooperation environment, conditions exist for large-scale, high-speed development in coming years. The window refers to bottlenecks in methodology and technology encountered at two levels: transformation from correlative discovery to causal mechanism analysis, and transformation from research-oriented resource knowledge accumulation to engineering product and measure application. Therefore, to seize opportunities and achieve breakthroughs, China should timely plan and layout the China Microbiome Initiative, selectively strengthen advantages, and promptly launch core research projects. Deepen interdisciplinary team collaboration, rely on convergence to enhance capabilities, overcome weaknesses, and foster formation of innovative scientific ideas and advanced technology platforms.

5.2 Basic Research Framework

In December 2016, Liu Shuangjiang, Zhao Guoping, and others organized the 582nd Xiangshan Science Conference on "China Microbiome Initiative," forming three basic principles for planning China' s microbiome initiative: (1) **National demand orientation**—multi-domain (industry, agriculture, medicine, environment) coverage: develop new microbiomics methods and technologies addressing China' s challenges in population health, environmental ecology, industrial and agricultural development, and marine strategy, understand and develop microbiome functions, and provide new ideas, products, and solutions for maintaining human and Earth's ecological health; (2) **Scientific hypothesis-driven**—multidisciplinary (mathematics, computing, physics, chemistry, biology) convergence: reveal organizational structure formation mechanisms, functional and structural material bases, stability and plasticity of microbiomes, species-environment interaction mechanisms, and cross-kingdom information exchange; (3) **Technological innovation support**—including innovation in research methods and technologies, and formation of disruptive technologies during research result transformation to serve strategic emerging industries.

According to the *National 13th Five-Year Plan (2016-2020)* and the *National Medium- and Long-Term Science and Technology Development Plan Outline (2006-2020)* issued by the State Council, and considering international microbiomics development trends and China' s specific conditions, the China Microbiome Initiative should focus on the following areas:

5.2.1 Human Microbiome The *National Medium- and Long-Term Science and Technology Development Plan Outline (2006-2020)* states that disease prevention and treatment should shift focus forward, adhering to prevention-first principles and combining health promotion with disease prevention. It also emphasizes strengthening Traditional Chinese Medicine (TCM) inheritance and innovation, developing and enriching TCM theory based on its theoretical inheritance and development through technological innovation and multidisciplinary integration. Increasing research shows that human health is closely related to microbiomes, including digestive, respiratory, reproductive, oral, and epidermal microbiomes—microbiomes are an inseparable part of the human body. Human microbiome research achievements will have major impacts in chronic disease prevention and control, sub-health conditioning, medical concept revolution, and new technology development. China has vast territory, and healthy populations of different ethnicities and regions may have characteristic microbiomes. Traditional Chinese Medicine is a treasure of the Chinese nation, and research shows that activation of effective TCM components requires participation of gut microorganisms. Analyzing mechanisms of mutualism and commensalism between healthy microbiomes and humans, pathogen-host cell and health microbiome cell interaction mechanisms, causal relationships between TCM efficacy and gut microbiome, and developing health maintenance and disease treatment and prevention technologies based on microbiomes are important human microbiome research contents that can promote healthy development of the TCM industry in conjunction with existing domestic and international research.

5.2.2 Environmental Microbiome (Soil, Water, Air) The *National Medium- and Long-Term Science and Technology Development Plan Outline (2006-2020)* lists comprehensive pollution control and waste resource utilization, fragile ecosystem function restoration and reconstruction, and marine ecology and environmental protection as development themes. Recently, China announced the "Water Ten Measures," "Air Ten Measures," and "Soil Ten

Measures" to build ecological civilization. Microorganisms are the main force in environmental governance and restoration and the foundation for maintaining ecosystem functions. Research on microbiome structure and function maintenance foundations, microbial community interaction and mechanisms affecting pollutant degradation and elimination, microbiome-environment factor interaction control, and environmental microbial agent development and application to serve black-odorous water body treatment, urban wastewater purification, contaminated soil remediation, and waste comprehensive utilization are important environmental microbiome research contents.

5.2.3 Crop Microbiome Food production security and crop quality improvement pose higher technological demands for China' s agricultural development. Microbiomes intimately associated with crops are important factors affecting crop growth, yield, and quality and represent the frontier of current life science research. The crop microbiome focuses on yield increase, disease resistance, and quality improvement of four staple grains and seven economic crops to serve "efficiency increase and input reduction." Combining rhizosphere microbiome, crop surface (leaf) microbiome, and endosymbiotic microbiome, research investigates microbiome impacts and regulatory mechanisms on important agronomic and medicinal traits of crops (rice, cotton, wheat, soybean, potato, vegetables, medicinal plants), including disease resistance, stress resistance, yield, and quality, analyzing regulatory functions of important biological compounds (such as hormones and volatile compounds) in microbiome-crop interactions. Research also examines microbiome impacts on crop continuous cropping obstacles and overcoming methods, and studies microbiomes affecting postharvest product quality, analyzing molecular mechanisms of complex infections and control. Based on this research, develop microbiome application technologies that can control important soil trait parameters, crop disease resistance, stress resistance, growth and quality, overcome continuous cropping obstacles, and improve soil quality, making important contributions to reducing fertilizer and pesticide use in crop production and improving Chinese agricultural product yield and quality.

5.2.4 Livestock Gut Microbiome Livestock is an important component of China' s agricultural production. Establishing technical systems suitable for livestock gastrointestinal microbiome research, systematically revealing impacts and pathways of livestock (pigs, dairy cows, poultry, etc.) breeds (genotypes) and feeding management on gastrointestinal microbiome composition and metabolism, studying host-microbiome interaction mechanisms, and developing microbiological application technologies that can improve feed resource conversion efficiency and production performance, enhance gastrointestinal function and host health, improve farming environmental quality, and product (meat, eggs, etc.) quality will significantly reduce or eliminate antibiotic use, promote ecological farming, comprehensively upgrade China' s livestock farming technology level, significantly improve farming efficiency, ensure product safety, improve ecological environment, and promote human health.

5.2.5 Industrial Microbiome (Traditional Fermentation, Bioleaching, Bioactive Substances) Microorganisms support the main body of modern industrial biotechnology. Upgrading industrial biotechnology and developing disruptive biotechnologies require guidance from microbial community (group) fermentation theory. The industrial microbiome will enhance traditional fermentation processes such as brewing and food fermentation industry efficiency and product quality, develop new raw materials, improve mineral mining capacity, and expand mineral resource reserves through developing mixed community fermentation, transformation, and production technologies. Research includes dynamic structure and function of microbiomes in China' s major traditional fermentation processes, revealing interspecies and inter-community interactions and co-evolution mechanisms with environmental factors; constructing synthetic functional microbial communities to replace traditional fermentation, providing theoretical and technical support and high-quality microbiome resources for upgrading traditional fermentation industries to standardized and automated modern fermentation processes; studying bioleaching microbiome-mineral interaction mechanisms to obtain microbial communities suitable for different regional (southern and northern) mineral deposits and environmental conditions, developing next-generation bioleaching technologies.

5.2.6 Marine Microbiome Based on the microbiome concept, revealing marine microbial metabolic processes, signal transduction connectivity, and metabolite formation mechanisms, developing marine microbial synthetic biology technology, releasing special metabolic pathways contained in typical marine ecosystem microbiomes, guiding discovery of metabolites, enzymes, energy, and other active substances, and discovering marine microbial drug lead compounds. Obtaining marine microorganisms that can effectively remove heavy metals or plastic pollution, discovering important genes (clusters) involved in removal or degradation of different heavy metals and plastics, constructing engineered bacteria that can effectively remove various common heavy metal and plastic pollution, and preliminarily establishing corresponding bioproduct process flows.

5.2.7 New Technology Platforms for Microbiome Research Methods and Applications Including high-throughput microbial cultivation technology, microbial community evolution display technology, and characterization technology for microbe-host and microbe-environment interactions.

5.2.8 Microbiome Data Storage and Functional Mining Establishing microbiome data standards and interface specifications, constructing microbiome big data storage and sharing platforms for effective data management and integration; developing new methods for microbiome big data processing, establishing high-quality microbiome reference databases, standardized data processing pipelines, and data analysis platforms; developing standard interfaces based on cloud computing, high-performance computing, and large-scale storage technology for microbiome big data processing and utilization, forming comprehensive application demonstration platforms for microbiome big data storage, integration, and development, establishing a "China Microbiome Initiative" data center, and achieving the leap from "data analysis" to "data science."

5.3 Specific Recommendations

1. **Plan and design the "China Microbiome Initiative (CMI)"as soon as possible**, implementing it in two phases. Phase 1: Promptly launch a batch of CMI pilot projects focusing on several major issues affecting national economy and people' s livelihood in health, agriculture, and environment, concentrating on 2-3 directions with Chinese characteristics and advantages for collaborative research. Simultaneously, strengthen technological innovation research and technology integration platform construction, particularly emphasizing data integration, analysis, and modeling platform construction. Phase 2: Establish a "China Microbiome Key Research and Development Program" with a scale of approximately 3 billion RMB, listing it as a priority development area in the 13th Five-Year Plan.

2. **Establish a China Microbiome Initiative expert group** in conjunction with China' s science and technology program management reform to conduct top-level planning, design, and layout for domestic and international microbiome science and technology development strategies and measures. Under the expert group' s leadership, and in combination with science and technology system reform, establish a lean operations team to support the expert group, identify several major directions and key scientific and technological issues, integrate relevant national scientific and technological forces, encourage innovative exploration while strengthening integrated research, and simultaneously enhance collaboration with various foreign scientific communities.

3. **Form a "concentrated research" project organization mechanism with firm direction, clear objectives, and flexible implementation.** Establish corresponding organizational mechanisms tailored to different research object systems—adapting to circumstances with concentrated objectives and converged efforts; implement in stages according to different research and development phases and content—adapting to trends with stable and continuous funding; determine scientific research questions based on different application goals—adapting to markets with translational research thinking, shifting from one-way "service" or one-way "achievement purchase" to two-way interaction between research and application; simultaneously adopt corresponding multi-channel funding mechanisms according to different R&D phases.

4. **Actively communicate and cooperate internationally, and promote participation in organizing the "International Microbiome Initiative."** Strive to influence international program organization with

scientific ideas and organizational models formed through our pilot research. In implementation strategy, prioritize regional microbiome cooperation programs along the "Belt and Road,"subsequently developing them into global cooperation programs.

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Note: Figure translations are in progress. See original paper for figures.