



Omics-driven and *in silico* approaches in probiotic research: current advances and translational potential

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Abstract

Probiotics are defined as live microorganisms that confer health benefits to the host; nevertheless, their therapeutic potential has been historically constrained by a reliance on phenotypic screening and generalized efficacy claims. This review shifts probiotic research toward a system-level understanding by highlighting the transformative impact of omics technologies and *in silico* approaches in overcoming these limitations. We examine how integrating genomics, transcriptomics, proteomics, and metabolomics can enable precise identification of strains, elucidate mechanisms of action, and reveal strain-specific functional properties often missed by conventional methodologies. A key focus of this review is the application of computational biology, including genome-scale metabolic models and artificial intelligence, which facilitates the predictive modeling of host–microbe interactions and accelerates the rational design of next-generation probiotics. The review further synthesizes recent insights regarding the role of these technologies in supporting personalized nutrition interventions that are specifically tailored to individual molecular profiles, while placing probiotics within the broader context of fermented foods and microbiota-modulating strategies. Finally, we address critical challenges – including issues related to data standardization, regulatory hurdles, and validation of *in silico* predictions – that must be resolved to translate these technological advances into safe, effective, and customized clinical applications.

Key words: probiotics, gut microbiota, fermented foods, omics technologies, *in silico* approaches, functional foods

Introduction

Probiotics, characterized as live microorganisms that confer health advantages to the host when administered in adequate amounts, have become a cornerstone in the domains of functional food science and preventive healthcare (Kerry et al. 2018). The human gastrointestinal tract harbors a complex and dynamic microbial ecosystem whose composition and metabolic activity play a critical role in host metabolism, immunity, and disease resistance (Żółkiewicz et al. 2020). Disruptions in this microbial balance, also known as dysbiosis, are increasingly implicated in multiple health problems, including obesity, diabetes, inflammatory bowel disease, and cardiovascular pathology (Sen 2019). Probiotics

help restore intestinal homeostasis through several mechanisms, including competitive exclusion of pathogens, enhancement of nutrient absorption, production of antimicrobial metabolites, and modulation of host immune responses (Dahiya and Nigam 2022).

The understanding of probiotics has substantially advanced since the initial observations made by Metchnikoff, who linked the longevity of Bulgarian peasants to their consumption of fermented milk products. According to modern definitions of probiotics, live organisms need to demonstrate strain-specific health benefits; this indicates a shift from generalized claims to evidence-based interventions (Ranjha et al. 2021). Although probiotics are widely incorporated into dairy-based



Figure 1. Global distribution of traditional fermented foods across major regions, illustrating the cultural diversity and prevalence of fermentation practices worldwide. Regions depicted include Central Asia (koumiss), West Africa (fermented cereals and legumes), Southeast Asia (tempeh and brem), East Asia (kimchi and gochujang), Eastern Europe and Russia (kefir), South Asia (gundruk), the Americas (fermented beverages), and Northeast Africa (ergo and garris)

fermented foods, their application has expanded into dietary supplements, non-dairy functional foods, and agricultural feed, underscoring their growing commercial and scientific relevance.

Fermented foods are an integral component of traditional diets across diverse geographical regions (Figure 1). Prominent examples include koumiss from Central Asia, fermented cereal- and legume-based foods from West Africa, soy-based products such as tempeh from Indonesia, dairy fermentations such as kefir from Russia, and vegetable-based preparations including kimchi from Korea (Ashaolu 2020; Jena and Panda 2023). The global distribution of these products underscores the cultural, nutritional, and functional significance of fermentation practices, which have historically formed the basis of probiotic science (Alemu and Kuyu 2024; Erem and Kilic-Akyilmaz 2024).

However, despite this rich historical context, a critical gap persists between the traditional, phenotype-based characterization of probiotics and the level of mechanistic understanding required for their clinical translation. Conventional screening methods, which utilize *in vitro* assays for acid tolerance, bile resistance, and antimicrobial activity, provide necessary but insufficient evidence for predicting *in vivo* efficacy. The emergence of high-throughput omics technologies coupled with advanced computational approaches has enabled us to bridge this gap, facilitating a system-level analysis

of probiotic functionality that was previously unattainable. This review critically examines how the convergence of multi-omics platforms and *in silico* tools is reshaping probiotic research, from strain discovery and mechanistic elucidation to personalized therapeutic applications.

Gut microbiota and probiotics

The increasing recognition of the essential role of gut microbiota in regulating physiological processes has prompted considerable interest in the rational design of next-generation probiotics (NGPs) (Baimakhanova et al. 2025). This imperative stems from the understanding that traditional phenotypic screening, while foundational, cannot adequately capture the genomic and metabolic complexity underlying probiotic efficacy. Omics technologies have enabled the sequencing and identification of safety-related genes at preliminary screening stages, thereby facilitating a more comprehensive and proactive evaluation of candidate probiotic strains (Haranahalli Nataraj et al. 2024).

The integration of genomics, transcriptomics, proteomics, and metabolomics with advanced computational frameworks has significantly enriched our knowledge of microbiome–host interactions (Sherwani et al. 2025). This multi-dimensional analytical approach not only reveals novel therapeutic targets but also improves the predictive accuracy of microbiome-based interventions.

Advanced simulation algorithms and AI-driven tools provide deeper insights into microbial metabolism, enabling precise probiotic optimization and supporting the development of personalized therapeutic strategies (Abdul Manan 2025; Baimakhanova et al. 2025).

The gut microbiota comprises a diverse array of bacterial genera with distinct functions (Figure 2). Beneficial taxa, including *Lactobacillus* and *Bifidobacterium*, help maintain intestinal barrier integrity, facilitate pathogen exclusion, and modulate immune responses. Conversely, an overabundance of potentially pathogenic genera such as *Clostridium*, *Fusobacterium*, and *Peptococcus* is linked with dysbiosis and various metabolic disorders (Zimbru et al. 2025). Probiotics restore homeostatic balance through competitive exclusion and production of inhibitory metabolites, particularly short-chain fatty acids.

Prebiotics, synbiotics, postbiotics, and pharmabiotics

Probiotics consist of live microorganisms, such as *Lactobacillus* and *Bifidobacterium*, that confer various health benefits through gut colonization and metabolite production, although their effectiveness may be influenced by viability and host-specific factors (Kaur 2025). Table 1 provides a comparative overview of probiotics, prebiotics, synbiotics, and postbiotics, with emphasis on their definitions, mechanisms of action, advantages, and limitations.

Prebiotics are indigestible food components or fibers that promote the growth of beneficial microorganisms in the human digestive system, particularly in the intestine and colon. They remain undigested following oral consumption and transit into the upper digestive

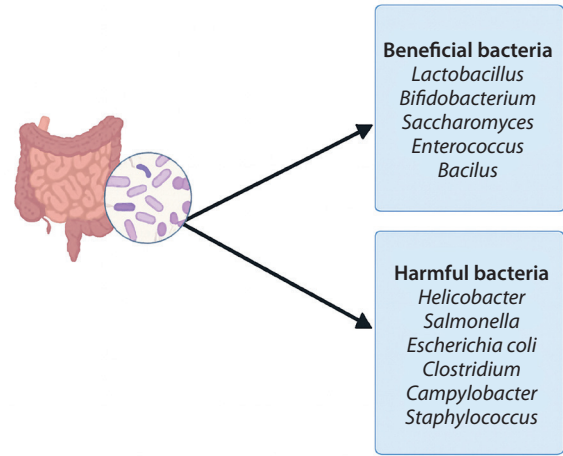


Figure 2. Schematic representation of the human gut microbiota ecosystem, depicting the balance between beneficial and potentially harmful bacterial genera. Beneficial taxa include *Lactobacillus* and *Bifidobacterium*, which contribute to maintaining intestinal barrier integrity, eliminating pathogens, and modulating immune response. Potentially harmful genera include *Clostridium*, *Fusobacterium*, and *Peptococcus*, whose overgrowth is associated with dysbiosis and metabolic disorders

tract, where they nourish the beneficial bacteria. Prebiotics, including inulin, fructooligosaccharides, and galactooligosaccharides, are nondigestible food components that selectively stimulate the growth of beneficial microorganisms (Davani-Davari et al. 2019).

Synbiotics, a combination of prebiotics and probiotics, synergistically enhance microbial survival and activity (Figure 3). They play a crucial role in achieving synergistic effects, enhancing microbial survival, and improving functional efficacy (Gomez Quintero et al. 2022).

Postbiotics are bioactive metabolites and microbial components produced during fermentation that exert

Table 1. Summary of key categories, functions, examples, and attributes of biotic family

Category	Definition	Examples	Mechanism	Advantages	Limitations
Probiotics	Live microorganisms	<i>Lactobacillus</i> , <i>Bifidobacterium</i> (Kaur 2025)	Direct colonization, metabolite production	Well-studied, diverse strains	Viability concerns, individual variation
Prebiotics	Nondigestible food components	Inulin, FOS, GOS (Deehan et al. 2024)	Selective growth stimulation	Stable, easy to incorporate	Indirect effects, GI discomfort
Synbiotics	Probiotic + prebiotic combination	<i>Lactocaseibacillus rhamnosus</i> + inulin (Davani-Davari et al. 2019; Gomez Quintero et al. 2022)	Synergistic enhancement	Improved efficacy	Complex formulation
Postbiotics	Metabolites/cell components	SCFAs, peptides, exopolysaccharide (Pawar et al. 2026)	Direct bioactive effects	No viability issues, safe	Limited research, standardization needed

FOS – fructooligosaccharides, GI – gastrointestinal, GOS – galactooligosaccharides, SCFAs – short-chain fatty acids.

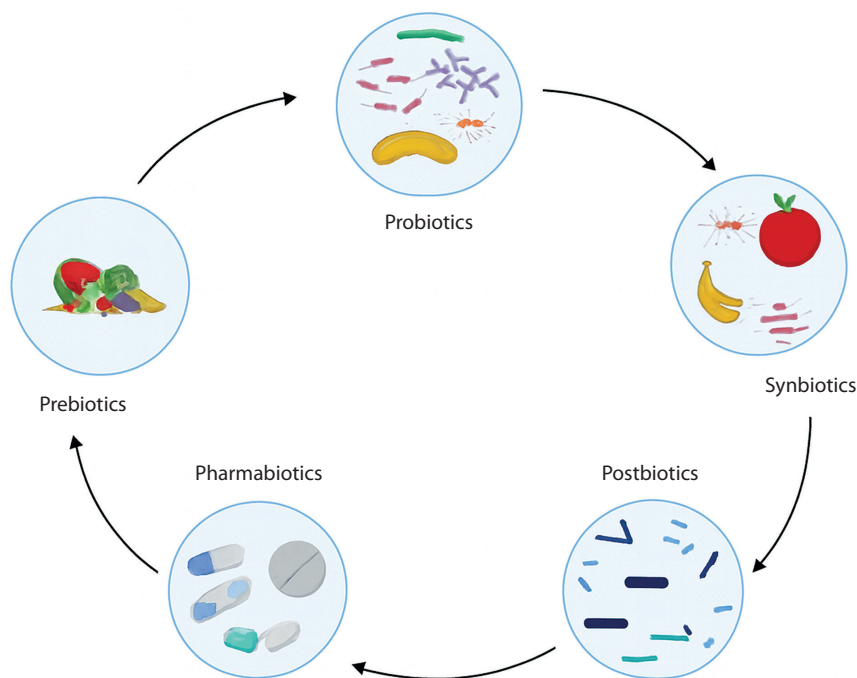


Figure 3. Overview of biotic family for microbiome modulation, illustrating the continuum from prebiotics and probiotics to synbiotics, postbiotics, and pharmabiotics

physiological effects without requiring live cells. Postbiotics comprise microbial metabolites and cellular components, such as short-chain fatty acids, peptides, and exopolysaccharides, which induce direct bioactive effects with increased safety and stability (Pawar et al. 2026).

Pharmabiotics refer to targeted therapeutic, microbe-based formulations designed for clinical applications (Wegh et al. 2019; Thorakkattu et al. 2022). Collectively, these categories represent a spectrum of microbiota-modulating interventions, ranging from substrate-driven prebiotic modulation to the direct bioactivity of postbiotic metabolites and clinically targeted pharmabiotics.

According to the definition of the International Scientific Association of Probiotics and Prebiotics, prebiotics are substrates that host microorganisms specifically use to confer health benefits (Ashaolu 2020; Deka et al. 2021). While prebiotics and probiotics function through distinct mechanisms, they both aim to enhance host health by altering the gut microbiota.

The preceding sections establish that the gut microbiota is a complex, functionally diverse ecosystem with significant therapeutic potential when modulated by probiotics, prebiotics, and related interventions. However, to fully realize this potential, it is essential to advance from descriptive characterization toward a mechanistic and system-level understanding of probiotic functionality.

The following sections examine how advanced omics technologies – spanning genomics, transcriptomics, proteomics, and metabolomics – are enabling this transition by providing high-resolution molecular insights into probiotic strain identity, gene expression, protein function, and metabolic output.

Omics technologies in probiotic research

The integration of advanced omics technologies and computational approaches has markedly improved our understanding of probiotics. Genomics enables precise strain identification, safety assessment by detecting virulence and antibiotic resistance genes, and metabolic pathway reconstruction. Transcriptomics reveals dynamic gene expression patterns under host-relevant conditions, whereas proteomics identifies functional proteins involved in adhesion, secretion, and host interaction. Metabolomics completes this system-level portrait by profiling various bioactive metabolites, such as short-chain fatty acids, vitamins, and antimicrobial peptides, which collectively represent the functional output of probiotic activity (Kwoji et al. 2023; Jo et al. 2025). Consequently, the application of multi-omics approaches is crucial to comprehensively understand probiotic effects, enabling the identification of microbial metabolites and their impact on host health (O'Connell 2020).

These technologies are equally vital to maintain quality assurance and facilitate safety surveillance in NGPs. Whole-genome sequencing and integrated multi-omics are critical for determining the safety and efficacy of novel probiotic candidates and engineered delivery systems (Uhegwu and Anumudu 2025). An interdisciplinary framework integrating omics-driven strain selection, engineered delivery systems, and personalized nutrition models has been proposed to bridge existing research gaps and advance the mechanistic understanding of diet–microbiota interactions for targeted probiotic therapies (Jadhav et al. 2026).

Multi-omics integration and computational frameworks

Each omics discipline provides a distinct but complementary perspective: genomics reveals the genetic potential of a given strain, transcriptomics captures its context-dependent gene expression pattern, proteomics identifies the functional protein machinery involved in specific biological processes, and metabolomics reflects the biochemical phenotype. Integrating these datasets with *in silico* approaches facilitates biomarker identification, elucidation of disease mechanisms, and prediction of therapeutic responses (Sibilio et al. 2025). Computational modeling and machine learning (ML) algorithms are becoming increasingly critical for interpreting these

complex, heterogeneous datasets and delivering practical biological insights (Mohr et al. 2024).

The full potential of omics technologies is achieved by integrating data from multiple molecular layers using computational frameworks (Figure 4). Emerging platforms, such as Graph Omics and Omics Analyst, provide integrative frameworks for the visualization and analysis of multi-omics data, facilitating disease prediction, diagnosis, and personalized treatment planning while addressing challenges of interoperability and scalability (Benabbou et al. 2026). Moreover, the convergence of omics with complementary technologies, including the Internet of Things and artificial intelligence (AI), extends the scope of personalized medicine toward proactive, predictive healthcare models. For instance, medical digital twins – created by merging omics data with continuous physiological monitoring and AI-driven analytics – simulate an individual's health status, enabling preemptive interventions tailored to the patient's molecular and physiological profiles (Verma et al. 2025).

Omics technologies and their application in probiotic research

The integration of omics technologies has fundamentally transformed probiotic research from a phenotype-driven approach to a system-level understanding of micro-

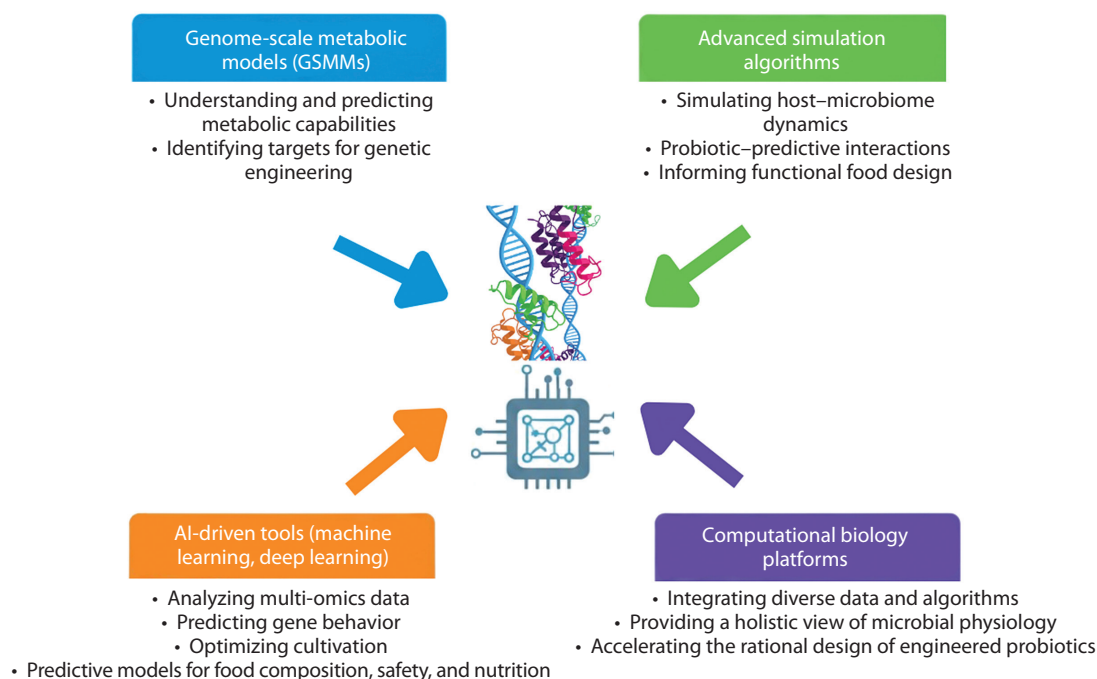


Figure 4. Computational frameworks supporting system-level analysis and engineering of probiotics, depicting the integration of multi-omics data through bioinformatics platforms, genome-scale metabolic models, and artificial intelligence-driven analytical tools

Table 2. Overview of omics approaches and their roles in advancing probiotic research

Omics technology	Application in probiotic research	Examples of recent insights	Advantages	Limitations	Comparison to traditional screening
Genomics	Strain identification, safety assessment (virulence and antibiotic resistance genes), metabolic pathway reconstruction	Identification of bacteriocin gene clusters in <i>Lactobacillus</i> ; metabolic modeling of <i>Escherichia coli</i> Nissle 1917 (Van Der Hof et al. 2022)	High resolution; comprehensive safety profiling; predictive capacity	Static data; requires bioinformatics expertise	Detects genetic safety risks and functional genes missed by traditional biochemical tests
Transcriptomics	Gene expression analysis under stress conditions and host interaction	Identification of stress-response genes and immune modulation pathways (He et al. 2025)	Dynamic insight into activity; regulatory network identification	Sensitive to handling; variability; high cost	Explains molecular mechanisms unlike traditional viability counts
Proteomics	Identification of proteins involved in adhesion, metabolism, and secretion	Discovery of S-layer proteins and functional enzymes (Künzel et al. 2023)	Direct functional insight; detects post-translational modifications	Technically complex; low-abundance detection challenges	Identifies functional proteins unlike basic adhesion assays
Metabolomics	Profiling metabolites such as SCFAs, vitamins, and bioactive compounds	Pinpointing SCFAs regulating immunity; identifying novel anti-inflammatory peptides (Yassin et al. 2025)	Direct phenotype linkage; clinically relevant	Complex data interpretation; instability; standardization needed	Reveals full metabolic output beyond simple biochemical tests

SCFAs – short-chain fatty acids.

bial functionality. While traditional methods mostly depend on *in vitro* assays, omics approaches provide a high-resolution map of the genetic and metabolic potential of probiotic strains. Table 2 summarizes the roles of each major omics technology in advancing probiotic research.

Comparative analysis: omics versus traditional probiotic screening

The transition from traditional screening to omics-driven approaches represents a significant paradigm shift in probiotic research. Traditional screening predominantly utilizes *in vitro* phenotypic assays, such as measuring acid and bile tolerance, antimicrobial activity by well diffusion methods, and surface hydrophobicity. Although these methods are cost-effective and provide the necessary initial data, they frequently show limitations in providing the required mechanistic depth and predictive capacity for *in vivo* efficacy.

Omics technologies overcome these limitations by enabling a “bottom-up” discovery process. For instance, while conventional screening might identify a strain that inhibits a pathogen, genomics and proteomics can reveal the mechanism underlying this inhibitory effect –

whether it occurs due to acid production, bacteriocin secretion, or competitive exclusion. Additionally, omics enables the discovery of NGPs that may not meet traditional criteria but possess genetic markers for specific therapeutic functions, such as anti-inflammatory properties (Baimakhanova et al. 2025). Nevertheless, the complexity and cost of omics technologies remain significant barriers, suggesting that an integrated approach – employing omics for discovery and mechanistic validation and traditional methods for quality control – represents the current gold standard for industrial applications.

The preceding discussion demonstrates that omics technologies generate extensive, multi-dimensional datasets that provide an unprecedented level of detail regarding probiotic strains. However, given the sheer volume and complexity of these data, robust computational frameworks are required to interpret and translate them into useful biological insights. The following section examines how *in silico* approaches, including genome-scale metabolic models (GSMMs), ML, and bioinformatics platforms, serve as essential analytical engines for converting raw omics data into predictive models of probiotic function and host–microbe interactions.

***In silico* and AI-based approaches**

The rapid accumulation of multi-omics data underscores the urgent need to establish robust computational frameworks for interpreting complex biological interactions. *In silico* approaches are now indispensable for bridging the gap between static genomic information and dynamic biological processes, providing predictive capacity that cannot be equaled by traditional *in vitro* methods.

GSMMs

The construction of GSMMs is at the core of *in silico* probiotic research. These models mathematically represent the entire metabolic network of microorganisms based on their genome annotations. By defining the stoichiometry of metabolic reactions, GSMMs allow researchers to simulate metabolic fluxes and predict growth behavior under various nutritional conditions, including the gut environment. GSMMs are used to identify essential nutrients for probiotic growth and to predict the secretion of beneficial metabolites such as short-chain fatty acids and vitamins.

A landmark study established the applicability of this approach by reconstructing a high-quality GSMM for the probiotic strain *Escherichia coli* Nissle 1917. This model successfully simulated the metabolic capabilities of the strain, identifying specific genes essential for its survival in the gut and predicting its competitive advantage over pathogens, thereby guiding the rational design of optimized therapeutic interventions (Van Der Hof et al. 2022). More recently, GSMMs have been applied in functional food biotechnology to optimize fermentation processes and enhance the biosynthesis of target bioactive compounds (Baimakhanova et al. 2025).

ML in microbiome analysis

While metabolic models are based on defined biochemical principles, ML and AI are adept in discerning patterns within vast, unstructured datasets. In probiotic research, ML algorithms are being increasingly applied to microbiome sequencing data to classify bacterial strains, predict functional outcomes, and stratify patient responses. ML has a critical role in predicting the interactions of specific probiotic strains with complex gut microbial communities. Deep learning models can analyze multi-omics data to discover novel probiotic candidates with high therapeutic potential, significantly reducing the time and cost of screening.

Furthermore, integrative ML frameworks have been developed to predict probiotic efficacy in disease management. By training models on large-scale clinical and metagenomic datasets, researchers can identify microbial biomarkers that can predict the host's response to a specific probiotic intervention, paving the way for personalized nutrition (D'Urso and Broccolo 2024). AI-driven tools are also used to predict the safety profiles of novel strains, identifying potential virulence factors or antibiotic resistance genes with higher accuracy than traditional alignment methods (Chisompola et al. 2026).

Bioinformatics tools for data integration

The utility of omics technologies largely relies on the bioinformatics pipelines used to process raw data. Open-source and web-based platforms, such as Graph Omics and Omics Analyst, provide user-friendly interfaces for integrating multi-omics data, enabling researchers to visualize correlations between gene expression and metabolite production and providing a system-level view of probiotic functionality (Papadaki et al. 2024). Standard pipelines for whole-genome sequencing analysis (e.g., Prokka and RAST) are now widely used for safety assessment, while comparative genomics tools help identify strain-specific genes that confer probiotic benefits, such as bacteriocin production clusters.

These computational strategies overcome the limitations of data heterogeneity and scale, enabling the transition from data generation to the derivation of actionable biological insights. They have significantly contributed to elucidate the mechanisms through which probiotics modulate host immunity by correlating specific microbial genes with host immunological markers (Yan and Polk 2011).

Collectively, these *in silico* approaches represent a paradigm shift from trial-and-error screening to rational and predictive design of probiotics. By combining the mechanistic precision of metabolic modeling with AI's pattern-recognition capabilities, researchers can accelerate the development of NGPs tailored for specific clinical outcomes.

The abovementioned computational tools substantially enhance the mechanistic understanding of probiotic function and establish a robust analytical foundation for translating multi-omics insights into individualized therapeutic strategies. By integrating host-specific molecular data with predictive models of probiotic activity,

these approaches enable the development of personalized probiotic interventions customized according to individual microbiome profiles, genetic backgrounds, and clinical needs. The next section examines the emerging applications of omics-driven and AI-guided personalized medicine in the field of probiotics.

Applications in personalized medicine

Omics technologies are being incorporated progressively into personalized medicine, as they offer a multi-dimensional understanding of an individual's molecular and biochemical profile. Genomics, transcriptomics, proteomics, and metabolomics collectively analyze different biological levels – from genetic code to gene expression, protein function, and metabolic states – enabling clinicians and researchers to better understand complex disease mechanisms and individual variability (Ikwelle et al. 2025).

This integration facilitates the development of precise therapeutic strategies by linking genetic predispositions to molecular phenotypes, thereby improving treatment efficacy and minimizing adverse effects of the treatment. For example, genetic data can identify disease risk variants, transcriptomics can reveal condition-specific gene expression changes, proteomics can discover aberrant protein interactions, and metabolomics can reflect dynamic biochemical responses. By combining these insights, personalized medicine can move beyond one-size-fits-all approaches to individually tailored clinical interventions (Sibilio et al. 2025).

In the context of specific diseases such as cancer, multi-omics integration reveals molecular drivers and biomarkers that can inform personalized prognosis and therapy selection (Chakraborty et al. 2024). Likewise, for chronic diseases such as type 2 diabetes, integrating omics with clinical data improves our understanding of complex disease mechanisms and supports the development of personalized management protocols (Song et al. 2012). The future of personalized probiotic medicine depends on overcoming several pivotal barriers, including data integration complexity, high costs, data privacy concerns, and the need for robust validation across diverse populations. Innovations in ML and AI are expected to enhance multi-omics data interpretation, while the use of open-source technologies may accelerate accessibility and implementation (Hasanzad et al. 2021).

Industrial and market perspectives

The global probiotic market has significantly expanded, largely influenced by the increasing consumer preference for functional foods and preventive health-care solutions. As of 2023–2024, the market value is estimated at approximately USD 65–70 billion, with projections indicating a compound annual growth rate of 7–8%, potentially surpassing USD 100 billion by 2030 (Abdul Manan 2025). This expansion is fueled by elevated post-pandemic awareness of immunity and gut health, diversification into non-dairy alternatives and convenient dosage forms, and broadening of applications across multiple domains, including animal feed, infant formula, and cosmetics (Sehrawat et al. 2022). Notably, the Asia-Pacific region is experiencing the most rapid growth, while the integration of omics-driven personalized nutrition is emerging as a premium market segment (Espitia et al. 2016).

Figure 5 presents a comprehensive overview of commercially used probiotic strains categorized according to genus, along with representative global brands and manufacturers, visually depicting the relationship between probiotic taxonomy and industry application. However, the industry faces critical challenges, including a gap between rapid product commercialization and the necessity for rigorous scientific validation, concerns regarding labeling accuracy and strain viability at end of shelf-life, and the proliferation of inadequately substantiated health claims (Wiegers et al. 2023; Uhegwu and Anumudu 2025). To sustain market growth, stakeholders must prioritize quality assurance, transparent labeling, and harmonization of efficacy standards with the omics-based evidence base discussed throughout this review.

Challenges and limitations

Probiotic research and development, particularly in the context of omics-driven and *in silico* approaches, faces several scientific, methodological, regulatory, and translational constraints. Addressing these challenges is crucial to fully realize the therapeutic efficacy and commercial potential of probiotics and related microbiota-modulating interventions.

Strain specificity and translational inconsistency

A significant limitation encountered during probiotic research is the specificity of effects associated



Figure 5. Overview of commercially utilized probiotic strains classified by genus and species, with corresponding global brands and manufacturers. Representative commercial products are mapped to each strain, highlighting the transition of laboratory-characterized strains into regulated consumer products across the food supplement and pharmaceutical sectors

with individual strains, which complicates the extrapolation of results across different strains, formulations, or host populations. Additionally, variations in study design, including dosage, intervention duration, age group, baseline microbiota, and comorbidities, further complicate meta-analyses and formulating evidence-based guidelines (McFarland et al. 2018).

Methodological heterogeneity and lack of standardization

Despite substantial advancements in omics technologies, there is no universally accepted standard for characterizing probiotics, assessing their efficacy, and evaluating their safety. Differences in sample collection, sequencing platforms, bioinformatic pipelines, and statistical analysis contribute to data heterogeneity, limiting cross-study comparability and hindering the discovery of robust biomarkers (McFarland et al. 2018).

Regulatory ambiguity and safety concerns

Regulatory frameworks for probiotics remain fragmented, particularly regarding their classification as food, dietary supplements, or pharmaceutical products. This ambiguity creates inconsistencies in safety requirements, health claim substantiation, and post-market surveillance across regions, thereby delaying their clinical translation. Although omics-based tools can identify virulence factors and antibiotic resistance genes at an early stage, their systematic integration into regulatory guidance is still in the developmental stage (Haranahalli Nataraj et al. 2024).

Omics and in silico limitations

While multi-omics and *in silico* models have improved our mechanistic insights, they have introduced various technical and interpretive challenges. Integrating large heterogeneous datasets requires sophisticated

computational frameworks; however, issues such as data scale, noise, batch effects, and interoperability continue to pose significant challenges. Moreover, genome-scale metabolic models and AI-driven prediction tools largely depend on model assumptions and database completeness, which may not fully capture *in vivo* complexity (Baião et al. 2025).

Host variability and personalized responses

Host-related factors, including genetics, immune status, diet, lifestyle, medication use, and pre-existing microbiota composition, strongly influence probiotic colonization, metabolite production, and subsequent clinical response. This inter-individual variability limits the feasibility of developing universal probiotic formulations and complicates clinical trial design. Although the concept of personalized omics-guided probiotic strategies is appealing, their implementation is constrained by high costs, data privacy concerns, and limited validation in diverse populations (Zhao et al. 2026).

Market dynamics and the evidence–practice gap

The accelerated growth of the global probiotic market has surpassed the accumulation of high-quality clinical evidence in certain areas, contributing to a widening evidence–practice gap. A slowdown in clinical trial activities, coupled with exaggerated or unverified commercial claims, may erode consumer and professional trust in the industry. Ensuring rigorous strain selection, transparent labeling, and harmonized regulatory oversight is essential to align market expansion with scientifically validated health benefits (Silva et al. 2017).

Future perspectives

Despite significant progress, several research gaps hinder the seamless translation of probiotic discoveries into clinical practice in humans. The following critical areas require focused attention to fully realize the potential of omics-driven probiotic science.

Standardization of multi-omics integration

A major obstacle is the heterogeneous nature of multi-omics datasets. Future efforts should prioritize the development of standardized bioinformatics pipelines that smoothly integrate genomic, transcriptomic, and metabolomic data. Although emerging platforms such as Graph

Omics and Omics Analyst represent steps toward this goal, universal standardization protocols should be developed to facilitate cross-study comparisons and robust biomarker discovery (Papadaki et al. 2024).

Rational design of NGPs

The future approach will involve shifting from traditional screening to the rational design of NGPs. *In silico* modeling allows to predict metabolic pathways before strain engineering. This precision engineering can create strains tailored for specific conditions, such as inflammatory bowel disease or metabolic syndrome, transitioning probiotics from general dietary supplements to regulated live biotherapeutic products (Wiegers et al. 2023).

AI-driven personalized nutrition

The integration of AI with medical digital twins offers a promising approach to address host variability. By simulating individual host–microbiome interactions, AI can predict patient response to specific probiotic interventions, enabling truly personalized nutritional strategies that move beyond the traditional one-size-fits-all approach (D’Urso and Broccolo 2024).

Validation of *in silico* predictions

Although computational models are robust, they rely on assumptions that may not fully capture the complexity of *in vivo* environments. A critical future direction is the rigorous validation of *in silico* predictions using randomized clinical trials. Ensuring that model-based optimizations translate into tangible health benefits is essential for gaining regulatory approval and clinical acceptance (Abdul Manan 2025).

Conclusions

This review underscores the pivotal role of omics and computational approaches in redefining the field of probiotic science. The integration of genomics, transcriptomics, proteomics, and metabolomics has transitioned the field from traditional phenotype-based screening to a system-level understanding of microbial functionality, enabling unprecedented strain-level precision based on specific genetic markers and metabolic outputs. Computational tools, particularly genome-scale metabolic models and AI-driven analytics, have advanced the field by facilitating the predictive modeling of host–microbe interactions and the rational design of NGPs.

With the global probiotic market approaching USD 100 billion by 2030, these advancements are critical for bridging the gap between commercial demand and rigorous clinical validation. While challenges regarding data standardization and regulatory harmonization persist, the convergence of biological data and computational power offers a clear trajectory for translating mechanistic discoveries into safe, effective, and personalized therapeutic interventions. Ultimately, the synergy between omics and *in silico* approaches promises to evolve probiotics from generalized functional foods into targeted, evidence-based therapeutics.

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Author contributions

K.P. designed this study. K.P. conducted the literature review and data curation. K.P. wrote the manuscript. K.P. and R.K. edited and reviewed the manuscript. M.G. contributed to the review and editing. All the authors have read and approved the final manuscript.

Conflict of interest

The authors declare that they have no conflict of interest.

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