



Bacterial Colonization of Human Skin: Mechanisms, Microbial Ecology, Host Interactions, Dysbiosis and Emerging Therapeutic Strategies—A Review

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Abstract

Human skin is a complex ecological interface that supports diverse microbial communities while simultaneously restricting invasion by pathogens. Bacterial colonization is shaped by anatomical site, sebum, moisture, pH, temperature, oxygen availability, host immunity, age, genetics, environmental exposure, hygiene and antimicrobial use. Classical culture-based studies identified common skin residents such as *Staphylococcus*, *Corynebacterium* and *Cutibacterium*, whereas 16S rRNA sequencing and shotgun metagenomics have revealed substantially greater taxonomic and functional diversity and highlighted strong site- and person-specific patterns. Colonization is not simply the presence of bacteria on the surface; organisms interact with keratinocytes, sebaceous glands, immune cells and other microbes, forming a dynamic system of competition, cooperation and metabolic exchange. Commensals can provide colonization resistance through nutrient competition, bacteriocins and other antimicrobial molecules, while some strains can become pathobionts when barrier function or microbial community structure is disturbed. Dysbiosis has been associated with acne, atopic dermatitis, wound infection and other inflammatory or infectious skin disorders. Importantly, strain-level variation may be more informative than species-level

abundance for understanding disease, as demonstrated for *Cutibacterium acnes* and *Staphylococcus aureus*. Emerging strategies include narrow-spectrum antimicrobials, bacteriophages, live biotherapeutic products, prebiotics, postbiotics, microbial transplantation and personalized microbiome profiling. This review summarizes current knowledge of bacterial colonization, emphasizes mechanisms and ecological context, discusses methodological limitations, and identifies research priorities required to translate skin microbiome science into safe and effective clinical interventions.

Keywords

Skin microbiome; bacterial colonization; *Cutibacterium acnes*; *Staphylococcus epidermidis*; *Staphylococcus aureus*; dysbiosis; metagenomics; microbiome therapeutics

Graphical Overview

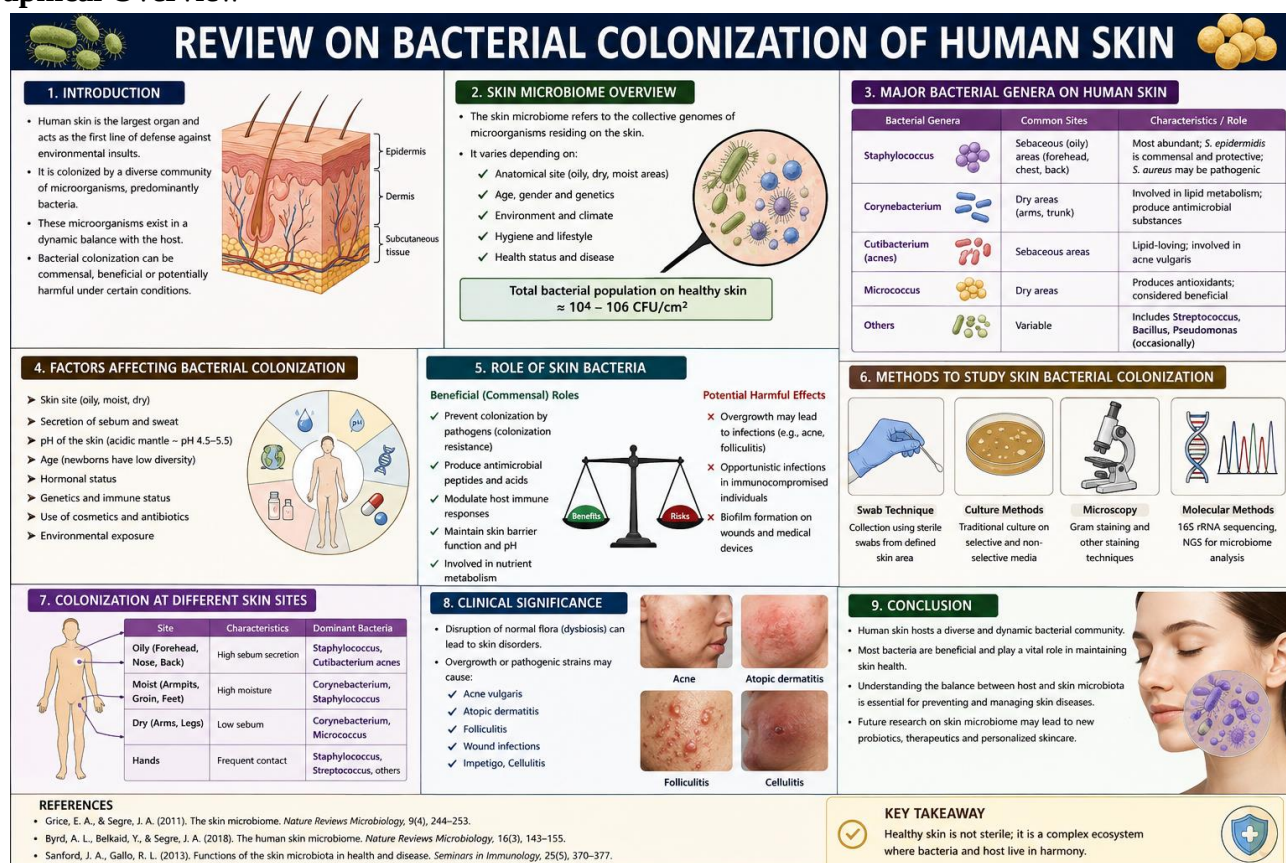


Figure 1. Overview of bacterial colonization, skin niches, major bacterial genera, study methods and clinical significance. Original schematic prepared for this manuscript.

1. Introduction

Human skin is both a physical barrier and a biologically active ecosystem. Its dry, acidic, relatively nutrient-poor surface is an unfavorable environment for many microorganisms, yet specialized niches around hair follicles and sweat and sebaceous glands support stable microbial communities. The composition of these communities varies markedly between sebaceous, moist and dry sites and also differs between individuals.

Bacterial colonization should be distinguished from infection. Colonization refers to the establishment and persistence of microorganisms without necessarily causing tissue damage or clinical disease. Infection

occurs when microbial growth and host responses result in tissue injury or systemic consequences. The same bacterial species can therefore behave as a harmless commensal in one context and as an opportunistic pathogen in another.

Modern microbiome research has shifted the field from species lists toward ecological and functional questions. Recent metagenomic studies can resolve microbial species, strains and metabolic pathways, while multi-omics approaches are beginning to connect community composition with host physiology and disease. This review focuses specifically on bacterial colonization, its determinants, host and microbial interactions, dysbiosis, methodological approaches and therapeutic opportunities.

2. Human Skin as a Microbial Ecosystem

The skin is heterogeneous rather than a single microbial habitat. Sebaceous sites such as the face, scalp and upper trunk contain lipid-rich environments that favor lipophilic organisms, particularly *Cutibacterium* species. Moist sites, including the axillae, groin and skin folds, favor *Corynebacterium* and *Staphylococcus*. Dry sites, such as the forearm and lower leg, generally contain lower microbial biomass but greater taxonomic diversity.

The physical and chemical properties of the stratum corneum impose strong selective pressure. Low water activity, acidic pH, fluctuating temperature, antimicrobial peptides and limited nutrients restrict many environmental organisms. Successful colonizers therefore possess adaptations for osmotic stress, desiccation, lipid utilization, adhesion and immune interaction. Hair follicles and glands provide protected microenvironments that differ substantially from the exposed epidermal surface.

The skin microbiome also changes over the lifespan. Early-life colonization is influenced by delivery mode, maternal and environmental exposure, while puberty produces major changes in sebum production and microbial ecology. Aging, lifestyle, climate, occupation, cosmetics and medications can further alter community structure.

3. Mechanisms of Bacterial Colonization

Colonization begins with exposure and physical or molecular attachment. Bacteria encounter corneocytes, extracellular matrix components, hair follicles and glandular secretions. Adhesins, surface proteins, lipoteichoic acids and other cell-envelope structures can promote attachment to host surfaces or to other microorganisms.

After attachment, bacteria must tolerate acidity, osmotic stress, antimicrobial molecules and nutrient limitation. *Staphylococci* can use multiple stress-response systems and surface structures to persist in the cutaneous environment. *Cutibacterium* is adapted to anaerobic, lipid-rich follicular niches and can metabolize sebaceous lipids. *Corynebacterium* species are well adapted to moist, nutrient-rich skin folds.

Persistence is also determined by microbial interactions. Bacteria compete for nutrients and attachment sites and may release bacteriocins, organic acids, enzymes or other inhibitory metabolites. Biofilms can increase persistence by creating structured communities with altered metabolic activity and protection from environmental stress. However, biofilm formation can also contribute to chronic infection when pathogenic or opportunistic organisms become established.

Colonization is therefore an ecological process involving attachment, adaptation, replication, competition, immune tolerance and long-term persistence. The outcome depends on both bacterial traits and the local host microenvironment.

4. Major Bacterial Colonizers

Staphylococcus is one of the most important skin-associated genera. Staphylococcus epidermidis is a dominant commensal on many individuals and can contribute to pathogen exclusion, immune education and barrier-associated functions. Staphylococcus aureus can also colonize healthy skin and nares, but particular strains have pathogenic potential and are important causes of skin and soft-tissue infection.

Cutibacterium acnes is strongly associated with sebaceous follicles. It is a normal resident of healthy skin and participates in lipid metabolism and microbial competition. Its association with acne is now understood as a strain- and community-level phenomenon rather than simple overgrowth of the species. Certain phylotypes and functional traits appear to be enriched in acne, while other strains are compatible with healthy skin.

Corynebacterium species are prominent in moist skin sites and can influence local metabolism and odor through interactions with sweat and skin lipids. Other organisms, including Micrococcus and various Proteobacteria, may contribute to site-specific communities, especially in dry or environmentally exposed areas.

5. Site-Specific Colonization and Ecological Determinants

Sebaceous niches are enriched in lipids and relatively low in oxygen, creating favorable conditions for Cutibacterium and selected Staphylococcus strains. Moist niches experience higher water availability and are influenced by sweat, friction and occlusion, supporting Corynebacterium and Staphylococcus. Dry sites impose stronger desiccation stress and show greater diversity.

Skin pH, sebum composition, sweat, temperature, oxygen tension and water activity are closely linked and should not be considered independently. Host factors such as age, sex-related hormonal changes, immune status and genetic variation can modify these microenvironments. Environmental factors including climate, occupational exposure, clothing, bathing and cosmetic use add another layer of variation.

An important implication is that a microbial profile from one body site cannot be assumed to represent the whole person. Standardized site selection and sampling are essential for comparing studies.

6. Host–Bacteria Interactions

Skin bacteria communicate with keratinocytes and immune cells through microbial molecules and metabolites. Commensals can stimulate controlled innate immune signaling and contribute to antimicrobial defense without causing pathological inflammation. The host in turn supplies nutrients, maintains the physical barrier and produces antimicrobial peptides that shape microbial selection.

Staphylococcus epidermidis illustrates this dual interaction particularly well. Evidence indicates that selected strains can promote immune surveillance and pathogen exclusion, whereas the same species can become an opportunistic pathogen in settings such as implanted medical devices or disrupted barriers. Thus, species identity alone is insufficient to predict biological behavior.

Staphylococcus aureus must overcome host antimicrobial peptides and immune responses to establish persistent colonization or infection. Its success is influenced by adhesins, immune-evasion mechanisms, toxins and strain-specific genomic features. The balance between commensal organisms and S. aureus can be particularly important in inflammatory skin disease.

7. Beneficial Functions and Colonization Resistance

Resident bacteria can protect the host through colonization resistance. Mechanisms include competition for nutrients and attachment sites, production of bacteriocins and other antimicrobial molecules, alteration of local pH, and modulation of host immune pathways. Some commensals can directly inhibit pathogens or prevent their expansion.

Colonization resistance is not absolute. It depends on community composition, bacterial strain traits, host barrier integrity and environmental conditions. Antibiotic exposure may remove susceptible commensals and create ecological space for resistant organisms. Inflammation can also alter nutrients and tissue conditions, potentially favoring organisms that are poorly represented in healthy skin.

The therapeutic implication is important: the objective should not always be complete eradication of bacteria. In many situations, restoring ecological balance may be more sustainable than broad-spectrum sterilization.

8. Dysbiosis and Skin Disorders

Dysbiosis refers broadly to a disturbed microbial community, including changes in composition, diversity, abundance or function. It is increasingly recognized as a component of several skin diseases, although association does not automatically establish causation.

In atopic dermatitis, lesional skin frequently shows reduced bacterial diversity and increased abundance of *Staphylococcus aureus*, particularly during flares. Barrier dysfunction, altered pH, inflammation and microbial virulence can reinforce one another, creating a positive feedback loop. Strain-level variation and prophage-associated genetic changes may further influence pathogenic behavior.

In acne, *Cutibacterium acnes* remains an important member of the follicular microbiome, but disease is not explained simply by the presence or total abundance of this species. Differences in phylotypes, strain functions and interactions with other microorganisms and host immunity appear more informative.

Other inflammatory conditions, including psoriasis and rosacea, and chronic wounds have also been associated with altered microbial communities. However, the field still needs longitudinal human studies to distinguish cause from consequence and to identify which microbial changes are drivers, markers or adaptations to disease.

9. Methods for Studying Skin Bacterial Colonization

Culture-dependent approaches remain valuable because they recover viable isolates for phenotypic testing, antimicrobial susceptibility assessment and whole-genome sequencing. Swab, tape-strip and follicular sampling can be used depending on the research question.

16S rRNA gene sequencing provides broad bacterial profiling but may have limited resolution at species or strain level and can be affected by primer bias. Shotgun metagenomics provides broader taxonomic and functional information and can support strain-level analyses, but skin samples are often low biomass and contain abundant host DNA, creating technical challenges.

Other approaches include quantitative PCR, whole-genome sequencing of isolates, metatranscriptomics, metabolomics and spatial methods. The choice of method should match the question: presence, abundance, viability, function, strain diversity and spatial localization are not interchangeable outcomes.

Important methodological challenges include low microbial biomass, contamination from reagents and the environment, differences in sampling depth, DNA extraction bias, sequencing platform differences and inconsistent bioinformatic pipelines. Negative controls and standardized protocols are therefore essential.

10. Strain-Level Diversity and Microbial Competition

Species-level abundance can conceal biologically important variation. *Cutibacterium acnes* is a classic example: acne and healthy skin can contain similar total amounts of the species while differing in strain or phylotype composition. Likewise, *Staphylococcus aureus* populations can differ in virulence genes, mobile genetic elements and adaptation to the inflammatory skin environment.

These findings support a shift from the question 'Which species are present?' to 'Which strains and functions are present, and what are they doing?' Strain-resolved metagenomics and isolate sequencing are increasingly important for this purpose. Functional validation in human-relevant models is needed to distinguish correlations from mechanisms.

11. Microbiome-Based Therapeutic Strategies

Microbiome-based therapy aims to modify disease-associated microbial functions while preserving beneficial community members. Potential approaches include live biotherapeutic products, topical probiotics, prebiotics, postbiotics, bacteriophages, narrow-spectrum antimicrobials and microbial transplantation.

Live biotherapeutic products are promising because selected commensals may directly compete with pathogens or produce antimicrobial molecules. However, efficacy depends on strain identity, formulation stability, dose, delivery site, host compatibility and long-term persistence.

Bacteriophages provide another route for selective targeting of bacterial strains while potentially sparing unrelated commensals. Narrow-spectrum antimicrobials and precision antimicrobial polymers are also being explored. These approaches may reduce collateral damage to the microbiome compared with broad-spectrum antibiotics.

Microbiome profiling could eventually support personalized treatment by identifying disease-associated strains, metabolic signatures or ecological states. Before clinical implementation, however, safety, reproducibility, manufacturing, resistance, regulatory classification and durable clinical benefit must be established.

12. Current Challenges and Research Gaps

Several gaps limit translation. First, many studies remain cross-sectional and cannot establish whether dysbiosis precedes disease or results from inflammation and treatment. Second, geographic, ethnic, age, sex, climate and lifestyle variation can make findings difficult to generalize. Third, different sampling and sequencing methods produce non-identical microbial profiles.

Fourth, microbial abundance does not necessarily equal microbial activity. Metabolomics and transcriptomics are needed to determine which organisms are functionally active. Fifth, strain-level heterogeneity remains incompletely characterized. Sixth, many experimental therapies have encouraging laboratory or small clinical datasets but limited evidence for long-term safety and efficacy.

Future studies should use standardized sampling, longitudinal designs, multi-omics, strain-resolved analysis, mechanistic validation and clinically meaningful endpoints. Greater integration of microbiology, dermatology, immunology, bioinformatics and pharmaceutical formulation science will be important.

13. Future Perspectives

The future of skin microbiome research is likely to be increasingly precision-oriented. Instead of treating all members of a bacterial species as equivalent, investigators may identify protective and disease-associated strains, their metabolites and their interactions with host cells.

Artificial intelligence and machine learning may assist in integrating microbial, clinical and environmental data to predict disease activity or treatment response, but models require large, diverse and well-annotated datasets. Spatial and single-cell approaches may reveal where microbial interactions occur within follicles, glands and epidermal structures.

From a pharmaceutical perspective, stable topical delivery systems for live microbes, phages, microbial metabolites or narrow-spectrum agents represent an important area of development. The long-term goal is not to create sterile skin, but to engineer or support a resilient microbial ecosystem that protects the host while minimizing pathogenic behavior.

14. Conclusion

Bacterial colonization of human skin is a dynamic ecological process governed by the interaction of microbial traits, skin microenvironment, host immunity and external exposures. The dominant bacterial communities differ across sebaceous, moist and dry sites, and individual strains can have markedly different effects despite belonging to the same species.

Modern sequencing has revealed that skin health and disease cannot be understood by simple pathogen lists. Colonization resistance, strain-level diversity, microbial competition and host-microbe communication are central concepts. Dysbiosis is associated with several dermatological disorders, but more longitudinal and mechanistic studies are needed to establish causality.

Emerging microbiome-based therapies—including live biotherapeutics, phage therapy, postbiotics and precision antimicrobials—offer the possibility of restoring microbial balance rather than broadly eliminating bacteria. Continued integration of microbiology, genomics, immunology and pharmaceutical technology should accelerate the development of safer and more personalized approaches to skin health.

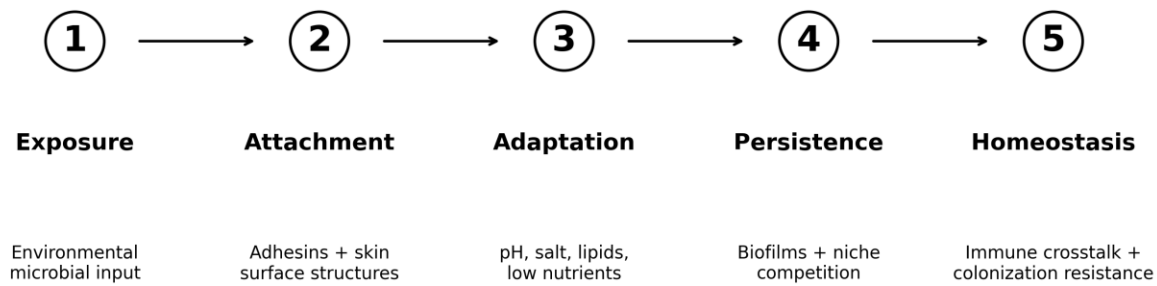
Figure 2. Conceptual sequence of bacterial colonization of human skin

Figure 2. Conceptual sequence of bacterial colonization of human skin, from exposure and attachment through adaptation, persistence and ecological homeostasis.

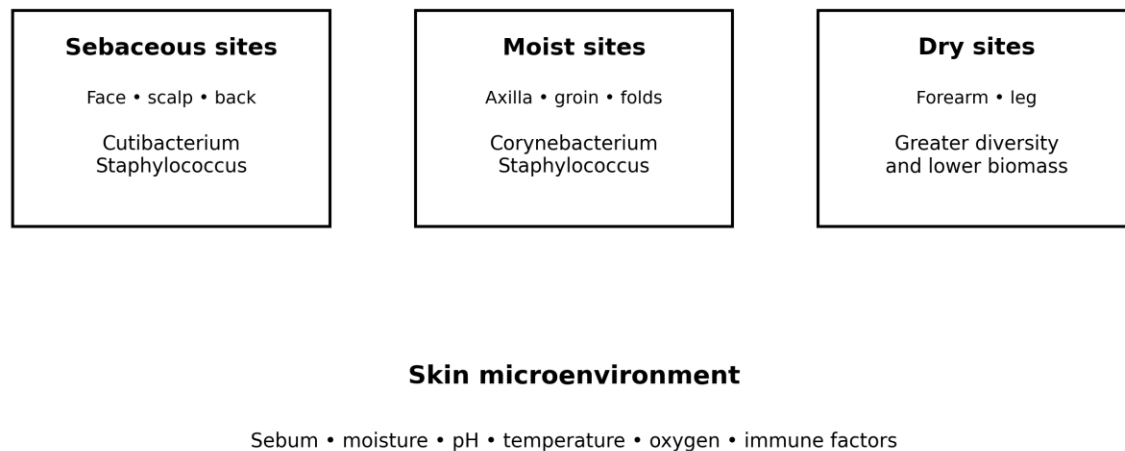
Figure 3. Site-specific ecology of bacterial colonization

Figure 3. Site-specific ecology of bacterial colonization. Sebaceous, moist and dry microenvironments select for different bacterial communities.

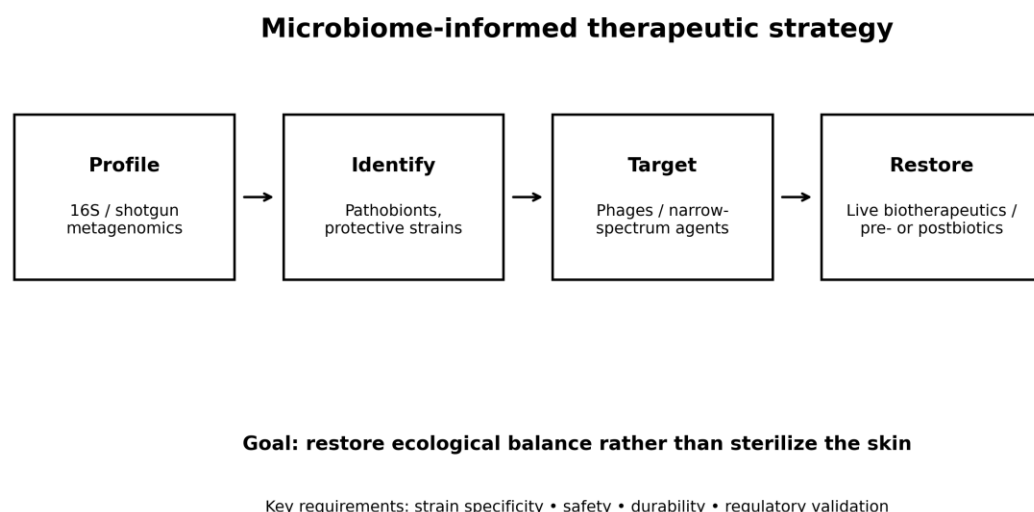
Figure 4. Translational pathway for microbiome-based interventions

Figure 4. Translational pathway for microbiome-based interventions, emphasizing profiling, strain/function identification, selective targeting and ecological restoration.

Table 1. Major bacterial groups associated with human skin

Bacterial group	Typical niche	Representative role	Clinical relevance
Staphylococcus	Moist, sebaceous, dry	Commensalism; immune interaction; competition	S. aureus colonization/infection; S. epidermidis opportunism
Cutibacterium	Sebaceous follicles	Lipid metabolism; niche competition	Strain-specific association with acne
Corynebacterium	Moist skin folds	Metabolism and community structure	May contribute to odor and opportunistic infection
Micrococcus and related taxa	Dry/exposed skin	Environmental adaptation; commensalism	Usually low clinical significance
Other Proteobacteria	Dry and exposed sites	High diversity; environmental interaction	Context-dependent opportunism

Table 2. Factors influencing bacterial colonization

Factor	Effect on skin ecology	Examples
Anatomical site	Determines local physicochemical niche	Face, axilla, forearm
Sebum	Provides lipids and favors lipophilic organisms	Sebaceous follicles
Moisture	Supports moisture-adapted taxa	Skin folds
pH	Selects acid-tolerant organisms	Acid mantle
Age/hormones	Changes sebum, barrier and immunity	Puberty, aging
Environment	Changes exposure and community composition	Climate, occupation
Hygiene/cosmetics	Can transiently alter abundance and composition	Cleansers, topical products
Antimicrobials	Can reduce susceptible organisms and alter community balance	Antibiotics, antiseptics

Table 3. Current and emerging methods

Method	Main output	Strength	Major limitation
Culture	Viable isolates	Phenotype, susceptibility, functional experiments	Misses unculturable/slow-growing taxa
16S rRNA sequencing	Bacterial community profile	Broad bacterial survey	Limited strain/function resolution
Shotgun metagenomics	Taxa + genes + pathways	Species/strain and functional potential	Low biomass and host-DNA contamination
Whole-genome sequencing	Genome of isolate	High-resolution strain analysis	Requires isolate recovery
Metatranscriptomics	Active transcripts	Functional activity	RNA stability and technical complexity
Metabolomics	Small-molecule profile	Links microbes to function	Metabolite attribution can be difficult

Table 4. Translational opportunities and key barriers

Approach	Potential advantage	Major research need
Live biotherapeutics	May restore protective functions	Strain selection, stability, safety and persistence
Bacteriophages	Selective bacterial targeting	Resistance, delivery, regulatory validation
Prebiotics/postbiotics	May support favorable ecology without live organisms	Standardization and clinical endpoints
Narrow-spectrum antimicrobials	Reduced collateral microbiome damage	Target specificity and resistance monitoring
Microbiota transplantation	Potential community-level restoration	Donor selection, safety and reproducibility
Personalized microbiome profiling	Treatment matched to microbial state	Validated biomarkers and cost-effective workflows

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Publication Note

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