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Microbial Influence on Animal Health: The Role of Gut Microbiota, Dysbiosis, and Probiotic Interventions

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Abstract

Microbes are integral to animal health, influencing various physiological processes and contributing to overall well-being. This review article explores the multifaceted roles of microbes in animal health, focusing on their diverse types, including bacteria, fungi, viruses, archaea, and protozoa. The gut microbiota is highlighted for its crucial functions in digestion, nutrient absorption, and immune system modulation. The article also examines the significance of skin, respiratory, and reproductive tract microbiota in maintaining health and preventing disease. Beneficial microbes and probiotics are discussed for their mechanisms of action, including immune modulation, pathogen exclusion, and metabolic contributions.

Microbial dysbiosis, or microbial imbalance, is identified as a key factor in the development of various diseases. This condition results from disruptions in microbial communities due to factors such as antibiotic use, poor diet, and environmental stressors. The review details common diseases linked to dysbiosis, including gastrointestinal, skin, respiratory, and metabolic disorders. Diagnostic techniques, including high-throughput DNA sequencing and quantitative PCR, are emphasized for their role in detecting and understanding dysbiosis.

The review concludes with a discussion on the importance of maintaining balanced microbial communities for health and the potential of targeted therapeutic approaches, such as probiotics, to restore microbial balance and improve health outcomes. Continued research is essential for advancing our understanding of microbe-host interactions and developing effective strategies for disease prevention and management.

Keywords: Microbial Dysbiosis, Gut Microbiota, Probiotics, Immune Modulation, Diagnostic Techniques

I. Introduction

Microorganisms, or microbes, play a crucial role in the health and well-being of all living organisms, including animals. These tiny entities, encompassing bacteria, viruses, fungi, archaea, and protozoa, are involved in various essential physiological processes. In animals, microbes contribute significantly to digestion, nutrient absorption, immune system development, and protection against pathogens. [1,2] The relationship between animals and

their resident microbes is the result of millions of years of co-evolution, emphasizing the indispensable role these microorganisms play in maintaining health. For instance, the gut microbiota aids in breaking down complex carbohydrates, synthesizing essential vitamins, and facilitating nutrient absorption, thereby directly influencing the nutritional status and overall health of the host. [3,4]

The importance of microbes extends beyond the gut. Skin and respiratory tract microbiota, for example, help protect against pathogenic invaders, enhance skin health, and maintain respiratory function. Microbes also interact with the immune system, aiding its development and modulating its responses to prevent overreactions that could lead to autoimmune diseases. [5,6] This intricate balance and interaction between microbes and their animal hosts underscore the critical role of these microorganisms in maintaining homeostasis and promoting health. [7-10]

The recognition of the significance of microbes in animal health dates to the late 19th and early 20th centuries, coinciding with the emergence of microbiology as a scientific discipline.[11] Early pioneers like Louis Pasteur and Robert Koch laid the groundwork for understanding microbial roles in disease and health. Pasteur's germ theory revolutionized the understanding of infectious diseases, while Koch's postulates provided a systematic approach to linking specific microbes to diseases. These foundational discoveries were pivotal in transforming the field of medicine and microbiology. [12,13]

However, it was not until the development of advanced molecular techniques in the late 20th and early 21st centuries that scientists could fully appreciate the complexity and diversity of microbial communities associated with animals. [14,15] Techniques such as DNA sequencing, metagenomics, and bioinformatics have enabled researchers to identify and study microbes that cannot be cultured in the laboratory, revealing a previously hidden world of microbial diversity. [16] This historical journey underscores the transition from viewing microbes solely as pathogens to recognizing their essential roles as mutualistic partners in animal health. [17,18] The objectives of this review are to provide a comprehensive overview of the interactive roles of microbes in animal health. By synthesizing current research, the review aims to elucidate the mechanisms through which microbes influence various aspects of animal physiology and health.[19] Key objectives include highlighting the beneficial roles of microbes, understanding the consequences of microbial imbalance or dysbiosis, and exploring current and future strategies for modulating microbial communities to enhance animal health. [20,21]

The scope of this review encompasses a wide range of animals, including domestic pets, livestock, and wildlife, ensuring the broad applicability of the findings. This comprehensive approach is essential for developing a holistic understanding of microbial roles in different animal species and environmental contexts.[22] The review will also consider practical applications in veterinary medicine, animal husbandry, and wildlife conservation, aiming to bridge the gap between fundamental research and real-world applications. By addressing these areas, the review will set a solid foundation for exploring the intricate and multifaceted roles of microbes in animal health, paving the way for a deeper understanding of this crucial aspect of biological science. [23,24]

II. Types of Microbes Involved in Animal Health

Microbes encompass a vast array of organisms that can be broadly categorized into bacteria, fungi, viruses, archaea, and protozoa. [25,26] Each of these groups plays distinct roles in animal health, contributing to both beneficial and pathogenic interactions. Understanding the specific contributions of these microbes is essential for comprehending their overall impact on animal health. [27]

Bacteria are perhaps the well-studied group of microbes in the context of animal health. Beneficial bacteria, such as those belonging to the genera Lactobacillus and Bifidobacterium, are integral components of the gut microbiota. [28] They aid in the digestion of complex carbohydrates, the production of essential vitamins, and the maintenance of a healthy gut barrier. [29,30] These bacteria also play a crucial role in modulating the immune system, helping to protect against pathogenic invaders. Conversely, pathogenic bacteria, such as Salmonella and Escherichia coli, can cause a range of diseases, from gastrointestinal infections to systemic illnesses, highlighting the dual nature of bacterial interactions with their hosts. [31,32 &33]

Fungi in the animal microbiome include both beneficial and harmful species. [34] Yeasts like Saccharomyces cerevisiae is known for their probiotic properties, contributing to gut health by enhancing digestion and nutrient absorption. [35] They also produce antimicrobial compounds that inhibit the growth of pathogenic microbes. On the other hand, pathogenic fungi such as Candida species can cause infections, especially in immunocompromised animals. [36,37] Fungal infections can range from superficial skin conditions to more severe systemic infections, illustrating the importance of a balanced fungal community in maintaining animal health. [38,39]

Viruses are unique among microbes in that they require a host cell to replicate. While often associated with diseases, viruses can also play beneficial roles. Bacteriophages, for instance, are viruses that infect and kill bacteria. [40,41] They can help control bacterial populations in the gut and other parts of the body, acting as natural predators of pathogenic bacteria. However, pathogenic viruses, such as those causing rabies or feline leukemia, can have devastating effects on animal health. The dual nature of viruses underscores their complex role in the microbial ecosystem of animals. [42-45]



Figure 1. Microbes-Animal Interactions

Archaea are a less commonly discussed group of microbes in the context of animal health, but they are significant nonetheless. [46] These microorganisms are particularly abundant in extreme environments, such as the gastrointestinal tracts of ruminants, where they play a crucial role in methanogenesis, the production of methane gas from the digestion of plant material.[47] This process is essential for the breakdown of complex carbohydrates in the diet of ruminants. While not typically pathogenic, the metabolic activities of archaea can influence the overall microbial ecosystem and impact animal health through their interactions with other microbes. [48,49]

Protozoa are single-celled eukaryotes that can have both beneficial and harmful effects on animal health. Beneficial protozoa, such as certain ciliates and flagellates in the rumen, assist in the digestion of fibrous plant materials, contributing to the nutritional status of their hosts. Pathogenic protozoa, such as Giardia and Toxoplasma, can cause significant health issues, including gastrointestinal disturbances and systemic infections. [50,51] The impact of protozoa on animal health is therefore highly variable, depending on the specific species and their interactions with the host. [52]

Overall, the balance between beneficial and pathogenic microbes is crucial for maintaining animal health. [53,54] Beneficial microbes contribute to essential physiological processes, including digestion, nutrient absorption, and immune modulation. [55-58] They also help protect against pathogenic invaders through competitive exclusion and the production of antimicrobial compounds. Conversely, pathogenic microbes can disrupt these processes, leading to disease and health deterioration. [59] Understanding the dynamic interactions between these microbial communities is essential for developing effective strategies to promote health and prevent disease in animals.[60]

By exploring the diverse roles of bacteria, fungi, viruses, archaea, and protozoa, we gain a comprehensive understanding of the complex microbial ecosystems that influence animal health. [61,62] This knowledge is vital for advancing veterinary medicine, improving animal husbandry practices, and enhancing wildlife conservation efforts. [63,64]

III.Microbial Colonization in Animals

Microbial colonization in animals is a complex and essential process that influences various aspects of their physiology and health. [65,66] Different microbial communities colonize distinct regions of the animal body, including the gut, skin, respiratory tract, and reproductive tract. [67,68] Each of these microbial ecosystems plays unique and critical roles in maintaining health, preventing disease, and supporting development. [69,70]

Gut Microbiota is one of the most extensively studied microbial communities in animals. It plays a crucial role in digestion and nutrient absorption by breaking down complex carbohydrates, proteins, and fats that the host cannot digest on its own.[71] The fermentation of dietary fibers by gut microbes produces short-chain fatty acids (SCFAs), such as acetate, propionate, and butyrate, which serve as energy sources for the host and help maintain gut health.[72,73] These microbial activities not only enhance nutrient availability but also contribute to the synthesis of essential vitamins, such as vitamin K and B vitamins, further supporting the host's nutritional status.[74.75]

In addition to its role in digestion, the gut microbiota has a significant impact on immune system development and function. [76,77] Early microbial colonization is crucial for the proper maturation of the immune system, training it to distinguish between harmful pathogens and benign or beneficial microbes. This process helps prevent autoimmune diseases and promotes immune tolerance.[78] Gut microbes also stimulate the production of mucosal antibodies and antimicrobial peptides, enhancing the gut's barrier function and protecting against infections.[79] Dysbiosis, or an imbalance in gut microbial communities, can lead to immune

dysregulation and increase susceptibility to various diseases, including inflammatory bowel disease and allergies.[80]

Animal	Dysbiosis	Disease	Example	References
Systems	Manifestation			
Gut	Decreased	Inflammatory	Reduced levels of	[81]
	microbial	Bowel Disease	Bacteroides and	
	diversity,	(IBD)	increased levels of	
	overgrowth of		Enterobacteriaceae in	
	pathogenic		IBD patients.	
	bacteria			
Gut	Overgrowth of	Antibiotic-	Disruption of normal	[82]
	Clostridium	associated	gut microbiota by	
	difficile	diarrhea	antibiotics leads to C.	
		(AAD)	difficile colonization	
			and toxin production.	
Skin	Reduced diversity	Atopic	Decreased levels of	[83]
	of skin microbiota,	dermatitis	Staphylococcus	
	overgrowth of		epidermidis and	
	Staphylococcus		increased levels of S.	
	aureus		<i>aureus</i> in atopic	
			dermatitis patients.	
Respiratory	Imbalance in	Pneumonia	Overgrowth of	[84,85]
Tract	respiratory		Streptococcus	
	microbiota,		<i>pneumoniae</i> or	
	increased		Haemophilus influenzae	
	colonization of		in the lungs.	
	pathogens			
Oral Cavity	Dysbiosis of oral	Periodontal	Increased levels of	[86]
	microbiota	disease	Porphyromonas	
			gingivalis and	
			Prevotella intermedia	
			associated with	
			periodontitis.	

Table 1. Microbial Colonization in animals

Skin Microbiota is another vital microbial community that contributes to animal health by protecting against pathogens and maintaining skin integrity. The skin is the first line of defense against environmental challenges, and its microbiota plays a key role in this protective function.[87] Beneficial skin microbes outcompete pathogenic organisms for resources and space, reducing the likelihood of infections. They also produce antimicrobial compounds that inhibit the growth of harmful bacteria, fungi, and viruses. Additionally, skin microbes influence the skin's immune responses, helping to modulate inflammation and promote wound healing. [88]

The influence of skin microbiota on skin health and disease prevention extends to conditions such as atopic dermatitis and other skin disorders. A balanced and diverse skin microbiota contributes to a robust skin barrier, preventing the colonization and invasion of pathogenic

organisms. [89] Conversely, disruptions in the skin microbiota can lead to increased susceptibility to infections and inflammatory skin conditions. Understanding the composition and functions of skin microbiota is essential for developing strategies to maintain healthy skin and prevent dermatological diseases in animals. [90]

Respiratory Tract Microbiota plays a critical role in respiratory health and disease resistance. [91,92] The upper and lower respiratory tracts host diverse microbial communities that interact with the respiratory epithelium and the immune system. These microbes help maintain respiratory homeostasis by preventing the colonization of pathogenic bacteria and viruses. [93,94] Beneficial respiratory microbes stimulate the production of mucus and antimicrobial peptides, which trap and neutralize inhaled pathogens. They also modulate immune responses, reducing the risk of excessive inflammation that can damage respiratory tissues. [95,96]

Respiratory tract infections, such as those caused by *Bordetella bronchiseptica* or *Mycoplasma* species, can disrupt the delicate balance of the respiratory microbiota, leading to disease.[97] Understanding the role of respiratory microbiota in health and disease can inform the development of preventive measures and treatments for respiratory conditions in animals.[98,99] Strategies such as probiotic supplementation and microbiota-targeted therapies hold promise for enhancing respiratory health and preventing infections.[100]

Reproductive Tract Microbiota has a profound influence on reproductive health and offspring development. [101] In females, the vaginal microbiota plays a key role in maintaining a healthy reproductive environment by producing lactic acid and other antimicrobial compounds that inhibit the growth of pathogens. [102] A healthy vaginal microbiota is associated with reduced risks of infections, such as bacterial vaginosis and sexually transmitted infections, which can impact fertility and pregnancy outcomes. During pregnancy, the maternal microbiota can influence the developing fetus's immune system and metabolic health, with implications for long-term health. [103,104]

In males, the reproductive tract microbiota is involved in maintaining a healthy balance that supports sperm health and fertility. Disruptions in the reproductive tract microbiota can lead to conditions such as prostatitis and epididymitis, affecting reproductive function.[105] Understanding the composition and functions of reproductive tract microbiota is essential for developing strategies to enhance reproductive health and address infertility issues in animals. Research in this area is still emerging, and further studies are needed to elucidate the complex interactions between reproductive tract microbiota and host health. [106]

In conclusion, microbial colonization in animals encompasses diverse and specialized communities that significantly impact health and disease. [107], The gut, skin, respiratory tract, and reproductive tract microbiota each play unique roles in supporting physiological functions, protecting against pathogens, and maintaining homeostasis. [108] Understanding these microbial ecosystems and their interactions with the host is crucial for advancing animal health and developing effective strategies to prevent and treat diseases. [109]

IV.Mechanisms of Microbe-Host Interaction

Microbes interact with their animal hosts through various complex mechanisms that are essential for maintaining health and preventing disease. [110] Key mechanisms include immune system modulation, metabolic contributions, and pathogen exclusion. [111]

Understanding these interactions provides valuable insights into how microbes influence host physiology and supports the development of strategies to enhance animal health. [112]

Immune System Modulation is a critical mechanism through which microbes influence host health. Beneficial microbes play a significant role in the development and function of the host's immune system. [113] They stimulate the maturation of immune cells and the production of immune molecules, helping the host to develop a robust and balanced immune response. [114] For instance, certain gut bacteria promote the production of regulatory T cells, which are essential for maintaining immune tolerance and preventing autoimmune diseases. [115] These microbes can also enhance immune responses by stimulating the production of antibodies and antimicrobial peptides, providing the host with better protection against infections. [116] On the other hand, some microbes can suppress immune responses to prevent excessive inflammation that can damage host tissues. This immune modulation ensures that the immune system can effectively respond to pathogens while avoiding harmful overreactions. [117] Table 2. Microbes-Animal Ineractions

System	Microflora	Interaction Type	Examples	References
Respiratory Tract	Streptococcus, Staphylococcus, Haemophilus, Neisseria	Commensal, Pathogenic	Normal microbiota helps prevent colonization by pathogens, but <i>Streptococcus</i> <i>pneumoniae</i> causes pneumonia.	[118]
Gut	Bacteroides, Bifidobacterium, Lactobacillus, Escherichia coli	Mutualistic, Commensal, Pathogenic	Gut bacteria aid digestion and immune function; E. coli is a commensal; <i>Salmonella causes</i> food poisoning.	[119]
Skin	Staphylococcus, Corynebacterium, Propionibacterium	Commensal, Pathogenic	Staphylococcus epidermidis is a normal skin resident; Staphylococcus aureus causes skin infections.	[120,121]
Urogenital System	Lactobacillus, Streptococcus, Staphylococcus	Commensal, Pathogenic	Lactobacillus in the female urogenital tract; Escherichia coli causing urinary tract infections.	[122]
Oral Cavity	Streptococcus, Actinomyces, Lactobacillus	Commensal, Pathogenic	Streptococcus mutans contribute to dental caries; Streptococcus pyogenes cause pharyngitis.	[123]

Metabolic Contributions of microbes are another vital aspect of their interaction with hosts. Microbes in the gut, for example, are involved in the breakdown and fermentation of complex carbohydrates, which the host cannot digest on its own. [124] This process produces shortchain fatty acids (SCFAs) like acetate, propionate, and butyrate, which serve as important energy sources for the host and have various health benefits. Butyrate is crucial for maintaining gut health as it provides energy to colonocytes and has anti-inflammatory properties. Additionally, microbes synthesize essential vitamins such as vitamin K and B vitamins, which are crucial for various metabolic processes in the host. These metabolic contributions are fundamental for the host's nutritional status and overall health, highlighting the indispensable role of microbial communities in maintaining metabolic homeostasis. [125,126]

Pathogen Exclusion is a mechanism by which beneficial microbes protect the host from infections. This occurs through competitive exclusion and the production of antimicrobial compounds. Beneficial microbes occupy ecological niches in the host, effectively outcompeting potential pathogens for space and resources. By establishing a stable microbial community, they prevent pathogenic organisms from gaining a foothold and causing disease.[127] Moreover, many beneficial microbes produce antimicrobial substances such as bacteriocins, organic acids, and hydrogen peroxide, which directly inhibit the growth of pathogens. For example, lactic acid bacteria in the gut produce lactic acid, lowering the pH and creating an inhospitable environment for many harmful bacteria.[128] This competitive exclusion and antimicrobial activity are crucial for maintaining a healthy microbial balance and protecting the host from infections. [129]

In conclusion, the mechanisms of microbe-host interaction, including immune system modulation, metabolic contributions, and pathogen exclusion, are essential for maintaining health and preventing disease in animals.[130] These interactions highlight the intricate and symbiotic relationship between microbes and their hosts, emphasizing the importance of a balanced and diverse microbial community. Understanding these mechanisms provides valuable insights into the fundamental roles of microbes in animal health and supports the development of innovative strategies to promote health and prevent disease through microbiota management. [131]

V.Beneficial Microbes and Probiotics

Probiotics are defined as live microorganisms that, when administered in adequate amounts, confer a health benefit on the host. [132] These beneficial microbes are primarily bacteria and yeasts that are naturally present in various environments, including the gastrointestinal tracts of animals. The most common types of probiotics include species from the genera *Lactobacillus, Bifidobacterium*, and *Saccharomyces. Lactobacillus* species are known for their ability to produce lactic acid, which helps maintain an acidic environment in the gut, inhibiting the growth of pathogenic bacteria. Bifidobacterium species are key players in the gut microbiota of mammals and contribute to the digestion of dietary fibers and the production of short-chain fatty acids. [133] *Saccharomyces boulardii*, a type of yeast, is also widely used as a probiotic due to its ability to survive stomach acid and colonize the intestines, where it can outcompete harmful microbes and enhance gut health. [134]

The mechanisms of probiotic action are diverse and multifaceted. Probiotics exert their beneficial effects through several pathways, including competitive exclusion of pathogens, enhancement of the gut barrier function, modulation of the immune system, and production of antimicrobial substances. [135] By colonizing the gut, probiotics compete with pathogenic microorganisms for nutrients and attachment sites, thereby preventing harmful bacteria from establishing themselves and causing infections. They also strengthen the gut barrier by

promoting the production of mucins and tight junction proteins, which help prevent the translocation of pathogens and toxins into the bloodstream. [136] Additionally, probiotics can modulate the host's immune system by stimulating the production of anti-inflammatory cytokines and enhancing the activity of immune cells such as macrophages and dendritic cells. [137] This immunomodulatory effect helps in maintaining immune homeostasis and preventing excessive inflammatory responses. Moreover, probiotics produce various antimicrobial compounds, including organic acids, hydrogen peroxide, and bacteriocins, which inhibit the growth of pathogenic bacteria and contribute to a balanced gut microbiota. [138]

Applications in veterinary medicine are broad and increasingly recognized for their potential to improve animal health and productivity. Probiotics are used in veterinary practice to prevent and treat a range of gastrointestinal disorders, including diarrhea, inflammatory bowel disease, and colitis. In livestock, probiotics are employed to enhance growth performance, improve feed efficiency, and reduce the incidence of infections, thereby minimizing the need for antibiotics and promoting sustainable farming practices. [139] For instance, probiotic supplements in poultry can help control *Salmonella* and *Campylobacter* infections, which are significant concerns for both animal health and food safety.[140] In companion animals, such as dogs and cats, probiotics are used to manage conditions like acute gastroenteritis and to support overall gut health. Additionally, probiotics have shown promise in improving reproductive health in breeding animals by modulating the vaginal microbiota and preventing infections that can impact fertility. The growing body of evidence supporting the benefits of probiotics in veterinary medicine underscores their importance as a natural and effective tool for enhancing animal health and well-being. [141]

VI. Microbial Dysbiosis and Animal Diseases

Microbial dysbiosis refers to an imbalance in the microbial communities residing in an animal's body, particularly within the gut, skin, or other mucosal surfaces. This imbalance can result from a variety of factors, including antibiotic use, poor diet, environmental stressors, infections, and underlying health conditions. [142] Antibiotics, while effective at eliminating pathogenic bacteria, can also disrupt beneficial microbial populations, leading to reduced diversity and an overgrowth of opportunistic pathogens. Dietary changes, especially those lacking in fiber and rich in processed foods, can negatively impact the gut microbiota by depriving beneficial microbes of essential nutrients.[143] Environmental stressors, such as overcrowding, poor sanitation, and exposure to toxins, can further exacerbate microbial imbalances. When the delicate equilibrium of microbial communities is disrupted, it can compromise the host's health, leading to various diseases and disorders. [144]

Common diseases linked to microbial imbalance encompass a broad spectrum of conditions affecting different organ systems. In the gastrointestinal tract, dysbiosis is closely associated with inflammatory bowel disease (IBD), irritable bowel syndrome (IBS), and chronic diarrhea. [145] These conditions often involve an overgrowth of harmful bacteria and a reduction in beneficial species, leading to inflammation, impaired nutrient absorption, and gastrointestinal discomfort. Beyond the gut, dysbiosis can also affect the skin, resulting in conditions like atopic dermatitis and other inflammatory skin disorders. In the respiratory tract, microbial imbalance can contribute to chronic respiratory diseases, including asthma and chronic obstructive pulmonary disease (COPD). [146] Additionally, dysbiosis has been linked to metabolic disorders such as obesity and diabetes, where alterations in the gut microbiota can influence host metabolism and insulin sensitivity. In reproductive health, an imbalance in the vaginal

microbiota can lead to bacterial vaginosis and other infections, affecting fertility and pregnancy outcomes. [147]

Diagnostic techniques for detecting dysbiosis have advanced significantly with the development of molecular and microbiological methods. [148] Traditional culture-based methods, while useful, are limited by the fact that many microbes are difficult to culture in the laboratory. [149] Modern techniques, such as high-throughput DNA sequencing and metagenomics, allow for comprehensive profiling of microbial communities, providing insights into the diversity and abundance of microbial species. These methods can identify specific microbial signatures associated with dysbiosis and disease. Quantitative PCR (qPCR) is another powerful tool that can quantify the presence of specific microbial groups and detect imbalances. [150] Additionally, advanced bioinformatics tools are used to analyze complex microbial data, helping to identify potential pathogenic shifts and microbial interactions. Stool samples, swabs from mucosal surfaces, and tissue biopsies are essential for accurately identifying dysbiosis, guiding treatment strategies, and monitoring the effectiveness of interventions aimed at restoring microbial balance. [151]

Microbial dysbiosis is a significant factor in the development of various animal diseases, stemming from disruptions in the balance of microbial communities due to antibiotics, diet, stress, and other factors. [152.153] The resulting conditions range from gastrointestinal and skin disorders to respiratory and metabolic diseases. Advances in diagnostic techniques, particularly molecular and metagenomic methods, have enhanced our ability to detect and understand dysbiosis, paving the way for targeted therapies and improved animal health management.[154]

7. Strategies for Modulating Microbiota

Modulating the microbiota through dietary interventions has gained considerable attention in recent years.[155] Prebiotics and dietary fibers are essential components in this strategy, as they serve as substrates for beneficial gut bacteria, promoting their growth and activity. Recent studies have shown that diets rich in prebiotics, such as inulin, fructooligosaccharides, and galactooligosaccharides, can enhance the abundance of beneficial bacteria like *Bifidobacteria* and *Lactobacillus*.[156] These changes in the gut microbiota composition can lead to improved gut health, enhanced immune function, and even potential benefits in mental health through the gut-brain axis. Moreover, dietary fibers, found in fruits, vegetables, and whole grains, have been associated with a lower risk of chronic diseases such as obesity, diabetes, and cardiovascular diseases due to their role in maintaining a healthy gut microbiome. [157,158]

Probiotic and synbiotic supplements are another effective strategy for modulating the microbiota. [159,160] Probiotics are live microorganisms that, when administered in adequate amounts, confer health benefits to the host. Common probiotic strains include *Lactobacillus* and *Bifidobacterium*, which have been extensively studied for their role in supporting digestive health, boosting the immune system, and even improving mood and mental health. [161,162] Synbiotics, which combine probiotics and prebiotics, offer a synergistic effect by enhancing the survival and colonization of beneficial microbes in the gut. Recent research has demonstrated that synbiotic supplements can improve gastrointestinal conditions, such as irritable bowel syndrome (IBS), and reduce inflammation, highlighting their potential to promote overall health. [163,164]

Antimicrobial stewardship and fecal microbiota transplantation (FMT) are critical in managing and restoring healthy microbiota, particularly in clinical settings. Antimicrobial stewardship focuses on reducing unnecessary antibiotic use, which is crucial as overuse and misuse of antibiotics can lead to dysbiosis, antibiotic resistance, and decreased microbiome diversity. [165] By implementing guidelines for appropriate antibiotic use and promoting alternative treatments, healthcare providers can help preserve the integrity of the microbiota. [166,167] FMT, which involves transferring fecal matter from a healthy donor to a recipient, has shown remarkable effectiveness in treating recurrent *Clostridium difficile* infections in humans and is gaining traction in veterinary practice.[168,169] Studies have demonstrated that FMT can restore healthy microbiota, alleviate gastrointestinal disorders, and even improve metabolic and immune functions in animals, underscoring its potential as a powerful tool for modulating microbiota in veterinary medicine. [170]

8. Future Directions in Microbiome Research

The future of microbiome research is poised to be revolutionized by emerging technologies and methodologies.[171] Advances in high-throughput sequencing, such as next-generation sequencing (NGS) and metagenomics, have significantly enhanced our ability to characterize the complex microbial communities residing in and on the human body. [172] Additionally, single-cell sequencing and multi-omics approaches, which integrate genomics, transcriptomics, proteomics, and metabolomics data, are providing a more comprehensive understanding of microbial functions and interactions.[173] Recent developments in computational tools and bioinformatics are enabling researchers to analyze vast amounts of microbiome data more efficiently, uncovering new insights into the roles of specific microbes and microbial genes in health and disease.[174]] These technological advancements are laying the groundwork for more precise and detailed microbiome studies, which could lead to novel diagnostic and therapeutic strategies. [175]

The potential for personalized microbiome-based therapies is an exciting frontier in microbiome research. [176] Personalized medicine aims to tailor treatments to an individual's unique genetic makeup, lifestyle, and microbiome composition. Recent studies suggest that individualized microbiome profiles could be used to predict responses to various treatments, including dietary interventions, probiotics, and medications. For example, research has shown that the efficacy of certain dietary supplements and drugs can vary significantly depending on an individual's microbiome. [177,178] Personalized microbiome-based therapies could also involve the development of custom probiotics or synbiotics designed to restore balance to a specific person's microbial community. [179,180] By leveraging the unique characteristics of everyone's microbiome, these tailored therapies have the potential to improve outcomes and reduce adverse effects in treating a wide range of conditions, from gastrointestinal disorders to metabolic diseases and beyond. [181]

As microbiome research advances, ethical considerations and challenges in microbiome manipulation are becoming increasingly important. One major concern is the potential for unintended consequences of altering the microbiome, which could disrupt the delicate balance of microbial communities and lead to negative health outcomes.[182] There are also ethical issues related to the collection, storage, and use of microbiome data, particularly regarding privacy and consent. [183,184] The possibility of using microbiome information for discriminatory purposes, such as in insurance or employment, raises additional ethical questions. [185,186] Moreover, the commercialization of microbiome-based products and therapies must be carefully regulated to ensure safety and efficacy. Addressing these ethical and regulatory challenges will be crucial to responsibly harnessing the potential of microbiome research for improving human health. By developing robust ethical guidelines and fostering

interdisciplinary collaboration, researchers can navigate these challenges and ensure that advancements in microbiome science benefit society.[187]

Conclusion

The intricate interplay between microbes and their animal hosts underscores the essential role that microbial communities play in maintaining health and preventing disease. This review has highlighted the diverse types of microbes, including bacteria, fungi, viruses, archaea, and protozoa, and their specific contributions to animal health. The detailed examination of gut, skin, respiratory, and reproductive tract microbiota reveals how these microbial communities influence digestion, immune function, pathogen exclusion, and overall well-being. Probiotics, as beneficial microbes, further illustrate the potential for harnessing microbial interactions to enhance health and prevent diseases through various mechanisms, including immune modulation and pathogen exclusion.

Microbial dysbiosis, characterized by imbalances in these microbial communities, has been linked to a range of diseases affecting multiple organ systems. Advances in diagnostic techniques, such as high-throughput sequencing and quantitative PCR, have improved our ability to identify and understand dysbiosis, offering insights into targeted therapeutic approaches. By recognizing the critical roles of microbes in health and disease, we can develop more effective strategies for managing and restoring microbial balance, ultimately leading to improved health outcomes in animals. Continued research in this field will be essential for refining these strategies and further elucidating the complex relationships between microbes and their hosts.

References

1.Pinnaka, A. K., & Tanuku, N. R. S. (2019). Marine microbial diversity for sustainable development. *Microbial Diversity in Ecosystem Sustainability and Biotechnological Applications: Volume 1. Microbial Diversity in Normal & Extreme Environments*, 117-158.

2.Sentenac, H., Loyau, A., Leflaive, J., & Schmeller, D. S. (2022). The significance of biofilms to human, animal, plant, and ecosystem health. *Functional Ecology*, *36*(2), 294-313.

3.Ahrodia, T., Das, S., Bakshi, S., & Das, B. (2022). Structure, functions, and diversity of the healthy human microbiome. *Progress in molecular biology and translational science*, *191*(1), 53-82.

4.Ambanpola, N., Seneviratne, K. N., & Jayathilaka, N. (2023). One Health Relationships in Microbe–Human Domain. *One Health: Human, Animal, and Environment Triad*, 147-160.

5.Shukla, R., Soni, J., Kumar, A., & Pandey, R. (2024). Uncovering the diversity of pathogenic invaders: insights into protozoa, fungi, and worm infections. *Frontiers in Microbiology*, *15*, 1374438.

6.Neish, A. S. (2009). Microbes in gastrointestinal health and disease. Gastroenterology, 136(1), 65-80.

7.Getzke, F., Thiergart, T., & Hacquard, S. (2019). Contribution of bacterial-fungal balance to plant and animal health. *Current opinion in microbiology*, *49*, 66-72.

8.Maritan, E., Quagliariello, A., Frago, E., Patarnello, T., & Martino, M. E. (2024). The role of animal hosts in shaping gut microbiome variation. *Philosophical Transactions of the Royal Society B*, *379*(1901), 20230071.

9.Pickard, J. M., Zeng, M. Y., Caruso, R., & Núñez, G. (2017). Gut microbiota: Role in pathogen colonization, immune responses, and inflammatory disease. *Immunological reviews*, 279(1), 70-89.

10. Alfaytouri, N. A., Al-Ryani, M. A., Gaballa, M. F., & Attitalla, I. H. (2024). Vulvovaginal Candidiasis In Pregnant Women. *GPH-International Journal of Biological & Medicine Science*, 7(03), 35-53.

11.Tewari, N., & Dey, P. (2024). Navigating Commensal Dysbiosis: Gastrointestinal Host-Pathogen Interplay in Orchestrating Opportunistic Infections. *Microbiological Research*, 127832.

12.Porter, N. T., & Martens, E. C. (2017). The critical roles of polysaccharides in gut microbial ecology and physiology. *Annual review of microbiology*, *71*(1), 349-369.

13.Bowater, L. (2016). The Microbiologists. The Microbes Fight Back: Antibiotic Resistance, 44.

14.Milgroom, M. G. (2023). The Germ Theory Paradigm. In *Biology of Infectious Disease: From Molecules to Ecosystems* (pp. 9-22). Cham: Springer International Publishing.

15. Reynolds, M. D., & from Space, R. MICROBES CAUSE DISEASE. Astronomy (July 2012), 52, 55.

16.Gest, H. (2010). Discovery and Exploration of the Microbial Universe: 1665 to" Modern Times".

17.Caumette, P., Bertrand, J. C., & Normand, P. (2015). Some historical elements of microbial ecology. *Environmental microbiology: Fundamentals and applications: Microbial ecology*, **18**.9-24.

19. Álvarez-Mercado, A. I., Navarro-Oliveros, M., Robles-Sánchez, C., Plaza-Díaz, J., Sáez-Lara, M. J., Muñoz-Quezada, S., ... & Abadía-Molina, F. (2019). Microbial population changes and their relationship with human health and disease. *Microorganisms*, 7(3), 68.

20.Ban, Y., & Guan, L. L. (2021). Implication and challenges of direct-fed microbial supplementation to improve ruminant production and health. *Journal of Animal Science and Biotechnology*, *12*(1), 109.

21.Gaballa, M. F. (2017). Chromobacterium Violaceum Strains Growth Conditions Impacting N-Acyl Homoserine Lactones AHL Production. Tennessee State University.

22.Shamoon, M., Martin, N. M., & O'Brien, C. L. (2019). Recent advances in gut microbiota mediated therapeutic targets in inflammatory bowel diseases: emerging modalities for future pharmacological implications. *Pharmacological Research*, *148*, 104344.

23.Gupta, A., Gupta, R., & Singh, R. L. (2017). Microbes and environment. *Principles and applications of environmental biotechnology for a sustainable future*, 43-84.

24.Lovell, C. R. (2003). Diversity, microbial. The Desk Encyclopedia of Microbiology, 326.

25.Gaballa, M. F. (2017). Chromobacterium Violaceum Strains Growth Conditions Impacting N-Acyl Homoserine Lactones AHL Production. Tennessee State University. Sobhana, K. S. (2024). Marine microbes: Taxonomy and diversity.

26.De Vos, W. M., Tilg, H., Van Hul, M., & Cani, P. D. (2022). Gut microbiome and health: mechanistic insights. *Gut*, 71(5), 1020-1032.

27.Papadimitriou, K., Zoumpopoulou, G., Foligné, B., Alexandraki, V., Kazou, M., Pot, B., & Tsakalidou, E. (2015). Discovering probiotic microorganisms: in vitro, in vivo, genetic and omics approaches. *Frontiers in microbiology*, *6*, 58.

28.Hornung, B., Martins dos Santos, V. A., Smidt, H., & Schaap, P. J. (2018). Studying microbial functionality within the gut ecosystem by systems biology. *Genes & nutrition*, *13*, 1-19.

29.Dey, P. (2019). Gut microbiota in phytopharmacology: A comprehensive overview of concepts, reciprocal interactions, biotransformations and mode of actions. *Pharmacological research*, *147*, 104367.

30.Bull, M. J. (2013). *Molecular genetic characterisation of probiotic bacteria: Lactobacillus acidophilus and Bifidobacterium species* (Doctoral dissertation, Cardiff University).

31.Vohra, A., Syal, P., & Madan, A. (2016). Probiotic yeasts in livestock sector. *Animal Feed Science and Technology*, 219, 31-47.

32.Roto, S. M., Rubinelli, P. M., & Ricke, S. C. (2015). An introduction to the avian gut microbiota and the effects of yeast-based prebiotic-type compounds as potential feed additives. *Frontiers in Veterinary Science*, *2*, 28.

33.Ezema, C., & Ugwu, C. C. (2015). Yeast (Saccharomyces cerevisiae) as a probiotic of choice for broiler production. *Beneficial microorganisms in agriculture, aquaculture and other areas*, 59-79.

34.Elghandour, M. M., Abu Hafsa, S. H., Cone, J. W., Salem, A. Z., Anele, U. Y., & Alcala-Canto, Y. (2024). Prospect of yeast probiotic inclusion enhances livestock feeds utilization and performance: An overview. *Biomass Conversion and Biorefinery*, *14*(3), 2923-2935.

35. Abid, R., Waseem, H., Ali, J., Ghazanfar, S., Muhammad Ali, G., Elasbali, A. M., & Alharethi, S. H. (2022). Probiotic yeast Saccharomyces: Back to nature to improve human health. *Journal of Fungi*, *8*(5), 444.

36.Bilal, R. M., Hassan, F. U., Saeed, M., Rafeeq, M., Zahra, N., Fraz, A., ... & Alagawany, M. (2023). Role of yeast and yeast-derived products as feed additives in broiler nutrition. *Animal Biotechnology*, *34*(2), 392-401.

37.Yadav, S., & Jha, R. (2019). Strategies to modulate the intestinal microbiota and their effects on nutrient utilization, performance, and health of poultry. *Journal of animal science and biotechnology*, *10*, 1-11.

38.Elhafi, G. E., Gaballa, M. F., Attitalla, I. H., & Albakush, S. A. (2024). Determination of Aflatoxin Levels in Groundnuts: A Comparative Study between Domestic and Imported Seed Supplies in Libya. *GPH-International Journal of Applied Science*, 7(04), 01-07.

39.Hanlon, G. W. (2007). Bacteriophages: an appraisal of their role in the treatment of bacterial infections. *International journal of antimicrobial agents*, *30*(2), 118-128.

40.Fernández, L., Duarte, A. C., Rodríguez, A., & García, P. (2021). The relationship between the phageome and human health: are bacteriophages beneficial or harmful microbes? *Beneficial microbes*, *12*(2), 107-120.

41.Pawar, A., & B.S. Yadav. (2024). Advancing Sustainability: Polyhydroxy Butyrate (PHB) Unveiled - A Comprehensive Review of Eco-friendly Applications. *Micro Environer*, *3*(02), 44–49. https://doi.org/10.54458/mev.v3i02.14142 (Original work published November 22, 2023)

42.Gorski, A., Dabrowska, K., Switala-Jeleń, K., Nowaczyk, M., Weber-Dabrowska, B., Boratynski, J., ... & Opolski, A. (2003). New insights into the possible role of bacteriophages in host defense and disease. *Medical Immunology*, *2*, 1-5.

43.Jamal, M., Bukhari, S. M., Andleeb, S., Ali, M., Raza, S., Nawaz, M. A., ... & Shah, S. S. (2019). Bacteriophages: An overview of the control strategies against multiple bacterial infections in different fields. *Journal of basic microbiology*, *59*(2), 123-133.

44.Sime-Ngando, T. (2014). Environmental bacteriophages: viruses of microbes in aquatic ecosystems. *Frontiers in microbiology*, *5*, 355.

45.Sharma, S., Chatterjee, S., Datta, S., Prasad, R., Dubey, D., Prasad, R. K., & Vairale, M. G. (2017). Bacteriophages and its applications: an overview. *Folia microbiologica*, *62*, 17-55.

46.Eckburg, Paul B., Paul W. Lepp, and David A. Relman. "Archaea and their potential role in human disease." *Infection and immunity* 71, no. 2 (2003): 591-596.

47.Moissl-Eichinger, C., Pausan, M., Taffner, J., Berg, G., Bang, C., & Schmitz, R. A. (2018). Archaea are interactive components of complex microbiomes. *Trends in microbiology*, *26*(1), 70-85.

48.Borrel, G., Brugère, J. F., Gribaldo, S., Schmitz, R. A., & Moissl-Eichinger, C. (2020). The host-associated archaeome. *Nature Reviews Microbiology*, *18*(11), 622-636.

49.Bang, C., Dagan, T., Deines, P., Dubilier, N., Duschl, W. J., Fraune, S., ... & Bosch, T. C. (2018). Metaorganisms in extreme environments: do microbes play a role in organismal adaptation? *Zoology*, *127*, 1-19. **50.**Cavicchioli, R. (2011). Archaea—timeline of the third domain. *Nature Reviews Microbiology*, *9*(1), 51-61.

51.Shinde, R. S., & Pawar, A. (2023). A Review on Production of Chitosan Nanoparticles from Shrimp Shells. *Micro Environer*, *3*(02), 28–35. https://doi.org/10.54458/mev.v3i02.14139

52.Berrouch, S., Escotte-Binet, S., Harrak, R., Huguenin, A., Flori, P., Favennec, L., ... & Hafid, J. (2020). Detection methods and prevalence of transmission stages of Toxoplasma gondii, Giardia duodenalis and Cryptosporidium spp. in fresh vegetables: a review. *Parasitology*, *147*(5), 516-532.

53.Moratal, S., Dea-Ayuela, M. A., Cardells, J., Marco-Hirs, N. M., Puigcercós, S., Lizana, V., & López-Ramon, J. (2020). Potential risk of three zoonotic protozoa (Cryptosporidium spp., Giardia duodenalis, and Toxoplasma gondii) transmission from fish consumption. *Foods*, *9*(12), 1913.

54.Tibayrenc, M. (1993). Entamoeba, Giardia and Toxoplasma: clones or cryptic species? *Parasitology Today*, *9*(3), 102-105.

55. Hohweyer, J., Dumètre, A., Aubert, D., Azas, N., & Villena, I. (2013). Tools and methods for detecting and characterizing Giardia, Cryptosporidium, and Toxoplasma parasites in marine mollusks. *Journal of food protection*, *76*(9), 1649-1658.

56.Dixon, B. R., Fayer, R., Santín, M., Hill, D. E., & Dubey, J. P. (2011). Protozoan parasites: Cryptosporidium, Giardia, Cyclospora, and Toxoplasma. *Rapid detection, characterization, and enumeration of foodborne pathogens*, 349-370.

57. Ashour, D. S., Saad, A. E., Dawood, L. M., & Zamzam, Y. (2018). Immunological interaction between Giardia cyst extract and experimental toxoplasmosis. *Parasite Immunology*, 40(1), e12503.

58.Ryan, U., Hijjawi, N., Feng, Y., & Xiao, L. (2019). Giardia: an under-reported foodborne parasite. *International Journal for Parasitology*, *49*(1), 1-11.

59.Yadav, S., & Jha, R. (2019). Strategies to modulate the intestinal microbiota and their effects on nutrient utilization, performance, and health of poultry. *Journal of animal science and biotechnology*, *10*, 1-11.

60. Elyass, M. E., Gaballa, M. F., Soutiyah, M. A., & Abid, A. A. D. (2021). Microbiological Evaluation and Chemical Analysis of Potable Water in Al-Jabal Al-Akhdar. *Albayan Scientific Journal*, (10), 439-429.

61. Anee, I. J., Alam, S., Begum, R. A., Shahjahan, R. M., & Khandaker, A. M. (2021). The role of probiotics on animal health and nutrition. *The Journal of Basic and Applied Zoology*, *82*, 1-16.

62.Adedokun, S. A., & Olojede, O. C. (2019). Optimizing gastrointestinal integrity in poultry: the role of nutrients and feed additives. *Frontiers in Veterinary Science*, *5*, 348.

63.Júnior, G. F. V., & Bittar, C. M. M. (2021). Microbial colonization of the gastrointestinal tract of dairy calves– a review of its importance and relationship to health and performance. *Animal Health Research Reviews*, 22(2), 97-108.

64.Vollaard, E. J., & Clasener, H. A. (1994). Colonization resistance. *Antimicrobial agents and chemotherapy*, *38*(3), 409-414.

65.Amat, S., Dahlen, C. R., Swanson, K. C., Ward, A. K., Reynolds, L. P., & Caton, J. S. (2022). Bovine animal model for studying the maternal microbiome, in utero microbial colonization and their role in offspring development and fetal programming. *Frontiers in Microbiology*, *13*, 854453.

66.Mulder, I. E., Schmidt, B., Lewis, M., Delday, M., Stokes, C. R., Bailey, M., ... & Kelly, D. (2011). Restricting microbial exposure in early life negates the immune benefits associated with gut colonization in environments of high microbial diversity. *PloS one*, *6*(12), e28279.

67.Davis, C. P., McAllister, J. S., & Savage, D. C. (1973). Microbial colonization of the intestinal epithelium in suckling mice. *Infection and Immunity*, 7(4), 666-672.

68.Zhang, K., Li, B., Guo, M., Liu, G., Yang, Y., Wang, X., ... & Zhang, E. (2019). Maturation of the goat rumen microbiota involves three stages of microbial colonization. *Animals*, *9*(12), 1028.

69.Hapfelmeier, S., Lawson, M. A., Slack, E., Kirundi, J. K., Stoel, M., Heikenwalder, M., ... & Macpherson, A. J. (2010). Reversible microbial colonization of germ-free mice reveals the dynamics of IgA immune responses. *Science*, *328*(5986), 1705-1709.

70.Wang, M., Wichienchot, S., He, X., Fu, X., Huang, Q., & Zhang, B. (2019). In vitro colonic fermentation of dietary fibers: Fermentation rate, short-chain fatty acid production and changes in microbiota. *Trends in Food Science & Technology*, 88, 1-9.

71.Koh, A., De Vadder, F., Kovatcheva-Datchary, P., & Bäckhed, F. (2016). From dietary fiber to host physiology: short-chain fatty acids as key bacterial metabolites. *Cell*, *165*(6), 1332-1345.

72.Wong, J. M., De Souza, R., Kendall, C. W., Emam, A., & Jenkins, D. J. (2006). Colonic health: fermentation and short chain fatty acids. *Journal of clinical gastroenterology*, 40(3), 235-243.

73.Vinelli, V., Biscotti, P., Martini, D., Del Bo', C., Marino, M., Meroño, T., ... & Riso, P. (2022). Effects of dietary fibers on short-chain fatty acids and gut microbiota composition in healthy adults: a systematic review. *Nutrients*, *14*(13), 2559.

74.Yang, J., Martínez, I., Walter, J., Keshavarzian, A., & Rose, D. J. (2013). In vitro characterization of the impact of selected dietary fibers on fecal microbiota composition and short chain fatty acid production. *Anaerobe*, *23*, 74-81.

75.Santana, P. T., Rosas, S. L. B., Ribeiro, B. E., Marinho, Y., & de Souza, H. S. (2022). Dysbiosis in inflammatory bowel disease: pathogenic role and potential therapeutic targets. *International journal of molecular sciences*, *23*(7), 3464.

76.Khalil, M. M., Gaballa, M. F., Sulaiman, G., & Attitalla, I. H. (2024). Epidemiological Assessment of the Burden and Determinants of Methicillin-Resistant Staphylococcus aureus (MRSA) Infections in Wounds. *GPH-International Journal of Biological & Medicine Science*, *7*(05), 39-50.

77.Aldars-García, L., Marin, A. C., Chaparro, M., & Gisbert, J. P. (2021). The interplay between immune system and microbiota in inflammatory bowel disease: a narrative review. *International journal of molecular sciences*, 22(6), 3076.

78.Pascal, M., Perez-Gordo, M., Caballero, T., Escribese, M. M., Lopez Longo, M. N., Luengo, O., ... & Mayorga, C. (2018). Microbiome and allergic diseases. *Frontiers in immunology*, *9*, 1584.

79.Polkowska-Pruszyńska, B., Gerkowicz, A., & Krasowska, D. (2020). The gut microbiome alterations in allergic and inflammatory skin diseases–an update. *Journal of the European Academy of Dermatology and Venereology*, *34*(3), 455-464.

80.Yoo, J. Y., Groer, M., Dutra, S. V. O., Sarkar, A., & McSkimming, D. I. (2020). Gut microbiota and immune system interactions. *Microorganisms*, *8*(10), 1587.

81.Carding, S., Verbeke, K., Vipond, D. T., Corfe, B. M., & Owen, L. J. (2015). Dysbiosis of the gut microbiota in disease. *Microbial ecology in health and disease*, *26*(1), 26191.

82.Skowron, K., Bauza-Kaszewska, J., Kraszewska, Z., Wiktorczyk-Kapischke, N., Grudlewska-Buda, K., Kwiecińska-Piróg, J., ... & Gospodarek-Komkowska, E. (2021). Human skin microbiome: impact of intrinsic and extrinsic factors on skin microbiota. *Microorganisms*, *9*(3), 543.

83.Prescott, S. L., Larcombe, D. L., Logan, A. C., West, C., Burks, W., Caraballo, L., ... & Campbell, D. E. (2017). The skin microbiome: impact of modern environments on skin ecology, barrier integrity, and systemic immune programming. *World Allergy Organization Journal*, *10*, 1-16.

84.Mahmud, M. R., Akter, S., Tamanna, S. K., Mazumder, L., Esti, I. Z., Banerjee, S., ... & Pirttilä, A. M. (2022). Impact of gut microbiome on skin health: gut-skin axis observed through the lenses of therapeutics and skin diseases. *Gut microbes*, *14*(1), 2096995.

85.Percival, S. L., Emanuel, C., Cutting, K. F., & Williams, D. W. (2012). Microbiology of the skin and the role of biofilms in infection. *International wound journal*, *9*(1), 14-32.

86.Patel, B. K., Patel, K. H., Huang, R. Y., Lee, C. N., & Moochhala, S. M. (2022). The gut-skin microbiota axis and its role in diabetic wound healing—a review based on current literature. *International journal of molecular sciences*, *23*(4), 2375.

87.Sharma, G., Khanna, G., Sharma, P., Deol, P. K., & Kaur, I. P. (2022). Mechanistic role of probiotics in improving skin health. *Probiotic Research in Therapeutics: Volume 3: Probiotics and Gut Skin Axis–Inside Out and Outside In*, 27-47.

88.De Pessemier, B., Grine, L., Debaere, M., Maes, A., Paetzold, B., & Callewaert, C. (2021). Gut-skin axis: current knowledge of the interrelationship between microbial dysbiosis and skin conditions. *Microorganisms*, *9*(2), 353.

89.Hrestak, D., Matijašić, M., Čipčić Paljetak, H., Ledić Drvar, D., Ljubojević Hadžavdić, S., & Perić, M. (2022). Skin microbiota in atopic dermatitis. *International journal of molecular sciences*, *23*(7), 3503.

90.Salem, I., Ramser, A., Isham, N., & Ghannoum, M. A. (2018). The gut microbiome as a major regulator of the gut-skin axis. *Frontiers in microbiology*, *9*, 1459.

91.Martínez, J. E., Vargas, A., Pérez-Sánchez, T., Encío, I. J., Cabello-Olmo, M., & Barajas, M. (2021). Human microbiota network: unveiling potential crosstalk between the different microbiota ecosystems and their role in health and disease. *Nutrients*, *13*(9), 2905.

92.Khambhaty, Y., & Samidurai, S. (2024). An insight into the microbiome associated with the damage of raw animal hide and skin-primarily protein, during leather making. *International Journal of Biological Macromolecules*, *264*, 130640.

93.Woo, Y. R., & Kim, H. S. (2024). Interaction between the microbiota and the skin barrier in aging skin: a comprehensive review. *Frontiers in Physiology*, *15*, 1322205.

94.Shah, T., Shah, Z., Baloch, Z., & Cui, X. (2021). The role of microbiota in respiratory health and diseases, particularly in tuberculosis. *Biomedicine & Pharmacotherapy*, *143*, 112108.

95.Elhafi, G. E., Gaballa, M. F., Attitalla, I. H., Albakush, S. A., & Albackoosh, M. A. (2024). Examining the Health Benefits of Olive Oil: A Review Tailored to the Libyan Setting. *GPH-International Journal of Biological & Medicine Science*, 7(04), 14-23.

96.Li, Z., Li, Y., Sun, Q., Wei, J., Li, B., Qiu, Y., ... & Ma, Z. (2022). Targeting the pulmonary microbiota to fight against respiratory diseases. *Cells*, *11*(5), 916.

97.Chotirmall, S. H., Gellatly, S. L., Budden, K. F., Mac Aogain, M., Shukla, S. D., Wood, D. L., ... & Hansbro, P. M. (2017). Microbiomes in respiratory health and disease: an Asia-Pacific perspective. *Respirology*, 22(2), 240-250.

98.Wypych, T. P., Wickramasinghe, L. C., & Marsland, B. J. (2019). The influence of the microbiome on respiratory health. *Nature immunology*, 20(10), 1279-1290.

99.Budden, K. F., Shukla, S. D., Rehman, S. F., Bowerman, K. L., Keely, S., Hugenholtz, P., ... & Hansbro, P. M. (2019). Functional effects of the microbiota in chronic respiratory disease. *The lancet Respiratory medicine*, *7*(10), 907-920.

100.de Steenhuijsen Piters, W. A., Sanders, E. A., & Bogaert, D. (2015). The role of the local microbial ecosystem in respiratory health and disease. *Philosophical Transactions of the Royal Society B: Biological Sciences*, *370*(1675), 20140294.

101. Esposito, S., & Principi, N. (2018). Impact of nasopharyngeal microbiota on the development of respiratory tract diseases. *European Journal of Clinical Microbiology & Infectious Diseases*, *37*, 1-7.

102.Lee-Fowler, T. (2014). Feline respiratory disease: what is the role of Mycoplasma species? *Journal of feline medicine and surgery*, *16*(7), 563-571.

103. Goodnow, R. A. (1980). Biology of Bordetella bronchiseptica. *Microbiological reviews*, 44(4), 722-738.

104. Akçakavak, G., Tuzcu, N., Özdemir, Ö., Tuzcu, M., Dağar, O., Tural, A., ... & Kanat, Ö. (2023). Diagnosis of Mycoplasma spp., Streptococcus spp., Bordetella bronchiseptica, Klebsiella spp., by Real-time PCR and Pathological Methods in Dogs with Bronchopneumonia. *Etlik Veteriner Mikrobiyoloji Dergisi*, *34*(2), 129-138.

105. Mattoo, S., & Cherry, J. D. (2005). Molecular pathogenesis, epidemiology, and clinical manifestations of respiratory infections due to Bordetella pertussis and other Bordetella subspecies. *Clinical microbiology reviews*, *18*(2), 326-382.

106. Akhreim, A. A., Gaballa, M. F., Sulaiman, G., & Attitalla, I. H. (2024). Biofertilizers Production and Climate Changes on Environmental Prospective Applications for some Nanoparticles Produced from some Microbial Isolates. *International Journal of Agriculture and Biosciences*, *13*(2), 196-203.

107. Johnson, L. R., Queen, E. V., Vernau, W., Sykes, J. E., & Byrne, B. A. (2013). Microbiologic and cytologic assessment of bronchoalveolar lavage fluid from dogs with lower respiratory tract infection: 105 cases (2001–2011). *Journal of Veterinary Internal Medicine*, *27*(2), 259-267.

108.Garbal, M., Adaszek, Ł., Łyp, P., Frymus, J., Winiarczyk, M., & Winiarczyk, S. (2016). Occurence of Bordetella bronchiseptica in domestic cats with upper respiratory tract infections. *Polish Journal of Veterinary Sciences*, *19*(2).

109.Dworkin, M. S., Sullivan, P. S., Buskin, S. E., Harrington, R. D., Olliffe, J., MacArthur, R. D., & Lopez, C. E. (1999). Bordetella bronchiseptica infection in human immunodeficiency virus-infected patients. *Clinical infectious diseases*, *28*(5), 1095-1099.

110.Feng, T., & Liu, Y. (2022). Microorganisms in the reproductive system and probiotic's regulatory effects on reproductive health. *Computational and structural biotechnology journal*, *20*, 1541-1553.

111. Appiah, M. O., Wang, J., & Lu, W. (2020). Microflora in the reproductive tract of cattle: a review. *Agriculture*, 10(6), 232.

112.Zhu, B., Tao, Z., Edupuganti, L., Serrano, M. G., & Buck, G. A. (2022). Roles of the microbiota of the female reproductive tract in gynecological and reproductive health. *Microbiology and Molecular Biology Reviews*, 86(4), e00181-21.

113.Kamińska, D., & Gajecka, M. (2017). Is the role of human female reproductive tract microbiota underestimated? *Beneficial Microbes*, 8(3), 327-343.

114.Li, J., McCormick, J., Bocking, A., & Reid, G. (2012). Importance of vaginal microbes in reproductive health. *Reproductive sciences*, *19*(3), 235-242.

115. Al-Nasiry, S., Ambrosino, E., Schlaepfer, M., Morré, S. A., Wieten, L., Voncken, J. W., ... & Kramer, B. W. (2020). The interplay between reproductive tract microbiota and immunological system in human reproduction. *Frontiers in immunology*, *11*, 378.

116.Chopra, C., Bhushan, I., Mehta, M., Koushal, T., Gupta, A., Sharma, S., ... & Sharma, S. (2022). Vaginal microbiome: considerations for reproductive health. *Future microbiology*, *17*(18), 1501-1513.

117.Gholiof, M., Adamson-De Luca, E., & Wessels, J. M. (2022). The female reproductive tract microbiotas, inflammation, and gynecological conditions. *Frontiers in Reproductive Health*, *4*, 963752.

118.Lehtoranta, L., Ala-Jaakkola, R., Laitila, A., & Maukonen, J. (2022). Healthy vaginal microbiota and influence of probiotics across the female life span. *Frontiers in microbiology*, *13*, 819958.

119.Venneri, M. A., Franceschini, E., Sciarra, F., Rosato, E., D'ettorre, G., & Lenzi, A. (2022). Human genital tracts microbiota: dysbiosis crucial for infertility. *Journal of Endocrinological Investigation*, *45*(6), 1151-1160.

120. Jendraszak, M., Skibińska, I., Kotwicka, M., & Andrusiewicz, M. (2024). The elusive male microbiome: revealing the link between the genital microbiota and fertility. Critical review and future perspectives. *Critical Reviews in Clinical Laboratory Sciences*, 1-29.

121.Colella, M., Topi, S., Palmirotta, R., D'Agostino, D., Charitos, I. A., Lovero, R., & Santacroce, L. (2023). An overview of the microbiota of the human urinary tract in health and disease: current issues and perspectives. *Life*, *13*(7), 1486.

122.Kaltsas, A., Zachariou, A., Markou, E., Dimitriadis, F., Sofikitis, N., & Pournaras, S. (2023). Microbial Dysbiosis and Male Infertility: Understanding the Impact and Exploring Therapeutic Interventions. *Journal of personalized medicine*, *13*(10), 1491.

123.Lv, S., Huang, J., Luo, Y., Wen, Y., Chen, B., Qiu, H., ... & Lu, R. (2024). Gut microbiota is involved in male reproductive function: a review. *Frontiers in Microbiology*, *15*, 1371667.

124. Chen, J., Chen, J., Fang, Y., Shen, Q., Zhao, K., Liu, C., & Zhang, H. (2023). Microbiology and immune mechanisms associated with male infertility. *Frontiers in Immunology*, *14*, 1139450.

125.Molina Morales, N. (2023). The microbiome of the male reproductive tract: uncovering its composition and origins.

126.Davies, R., Minhas, S., & Jayasena, C. N. (2023). Next-generation sequencing to elucidate the semen microbiome in male reproductive disorders. *Medicina*, 60(1), 25.

127. Moran, N. A., Ochman, H., & Hammer, T. J. (2019). Evolutionary and ecological consequences of gut microbial communities. *Annual Review of Ecology, Evolution, and Systematics*, *50*(1), 451-475.

128. Marshall, B. M., & Levy, S. B. (2011). Food animals and antimicrobials: impacts on human health. *Clinical microbiology reviews*, *24*(4), 718-733.

129.Hoffmann, A. R., Proctor, L. M., Surette, M. G., & Suchodolski, J. S. (2016). The microbiome: the trillions of microorganisms that maintain health and cause disease in humans and companion animals. *Veterinary pathology*, *53*(1), 10-21.

130.Kelly, D., King, T., & Aminov, R. (2007). Importance of microbial colonization of the gut in early life to the development of immunity. *Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis*, 622(1-2), 58-69.

131.Casadevall, A., & Pirofski, L. A. (2000). Host-pathogen interactions: basic concepts of microbial commensalism, colonization, infection, and disease. *Infection and immunity*, *68*(12), 6511-6518.

132. Neish, A. S. (2009). Microbes in gastrointestinal health and disease. Gastroenterology, 136(1), 65-80.

133.Petersen, C., & Round, J. L. (2014). Defining dysbiosis and its influence on host immunity and disease. *Cellular microbiology*, *16*(7), 1024-1033.

134.Bello, M. G. D., Knight, R., Gilbert, J. A., & Blaser, M. J. (2018). Preserving microbial diversity. Science, 362(6410), 33-34.

135.Braga, R. M., Dourado, M. N., & Araújo, W. L. (2016). Microbial interactions: ecology in a molecular perspective. *brazilian journal of microbiology*, 47, 86-98.

136. Weiland-Bräuer, N. (2021). Friends or foes-microbial interactions in nature. Biology, 10(6), 496.

137.Bosch, T. C., Guillemin, K., & McFall-Ngai, M. (2019). Evolutionary "experiments" in symbiosis: the study of model animals provides insights into the mechanisms underlying the diversity of host–microbe interactions. *BioEssays*, *41*(10), 1800256.

138. Eisthen, H. L., & Theis, K. R. (2016). Animal-microbe interactions and the evolution of nervous systems. *Philosophical Transactions of the Royal Society B: Biological Sciences*, *371*(1685), 20150052.

139.Lerouge, I., & Vanderleyden, J. (2002). O-antigen structural variation: mechanisms and possible roles in animal/plant-microbe interactions. *FEMS microbiology reviews*, *26*(1), 17-47.

140.Reem, M., & El-Seifat, S. (2023). The Role of Marine Algae as a Bioindicator in Assessing Environmental Pollution. *Journal of Survey in Fisheries Sciences*, 1837-1869.

141.Douglas, A. E. (2018). *Fundamentals of microbiome science: how microbes shape animal biology*. Princeton University Press.

142. Davis, S. L. (1998). Environmental modulation of the immune system via the endocrine system. *Domestic Animal Endocrinology*, *15*(5), 283-289.

143.Provenza, F. D., & Villalba, J. J. (2010). The role of natural plant products in modulating the immune system: an adaptable approach for combating disease in grazing animals. *Small Ruminant Research*, *89*(2-3), 131-139.

144.Song, L., Wang, L., Zhang, H., & Wang, M. (2015). The immune system and its modulation mechanism in scallop. *Fish & shellfish immunology*, *46*(1), 65-78.

145.SHAVIT, Y. (1991). Stress-induced immune modulation in animals: opiates and endogenous opioid peptides. In *Psychoneuroimmunology* (pp. 789-806). Academic Press.

146.Walker, C. G., Meier, S., Littlejohn, M. D., Lehnert, K., Roche, J. R., & Mitchell, M. D. (2010). Modulation of the maternal immune system by the pre-implantation embryo. *BMC genomics*, *11*, 1-13.

147.Kusnecov, A. W., & Rossi-George, A. (2002). Stressor-induced modulation of immune function: a review of acute, chronic effects in animals. *Acta Neuropsychiatrica*, *14*(6), 279-291.

148.Broom, L. J., & Kogut, M. H. (2018). Gut immunity: its development and reasons and opportunities for modulation in monogastric production animals. *Animal health research reviews*, 19(1), 46-52.

149.Dan, G., & Lall, S. B. (1998). Neuroendocrine modulation of immune system. *Indian journal of pharmacology*, *30*(3), 129-140.

150. Akhreim, A. A., Jadhav, A. U., Gaballa, M. F., Ahire, K. D., Abid, A. A. D., Sulaiman, G., & Attitalla, I. The Contribution of Stress-Tolerant Plant Growth-Promoting Rhizobacteria (PGPR) from Abiotic-Stressed Ecosystems to Sustainable Plant Management: A Comprehensive Review.

151.Rowland, I., Gibson, G., Heinken, A., Scott, K., Swann, J., Thiele, I., & Tuohy, K. (2018). Gut microbiota functions: metabolism of nutrients and other food components. *European journal of nutrition*, *57*, 1-24.

152.McFall-Ngai, M., Hadfield, M. G., Bosch, T. C., Carey, H. V., Domazet-Lošo, T., Douglas, A. E., ... & Wernegreen, J. J. (2013). Animals in a bacterial world, a new imperative for the life sciences. *Proceedings of the National Academy of Sciences*, *110*(9), 3229-3236.

153.Lourenço, M., Ramos-Morales, E., & Wallace, R. J. (2010). The role of microbes in rumen lipolysis and biohydrogenation and their manipulation. *Animal*, *4*(7), 1008-1023.

154.Callaway, T. R., Edrington, T. S., Anderson, R. C., Harvey, R. B., Genovese, K. J., Kennedy, C. N., ... & Nisbet, D. J. (2008). Probiotics, prebiotics and competitive exclusion for prophylaxis against bacterial disease. *Animal health research reviews*, *9*(2), 217-225.

155.Chiu, L., Bazin, T., Truchetet, M. E., Schaeverbeke, T., Delhaes, L., & Pradeu, T. (2017). Protective microbiota: from localized to long-reaching co-immunity. *Frontiers in immunology*, *8*, 1678.

156.Khan, I., Bai, Y., Zha, L., Ullah, N., Ullah, H., Shah, S. R. H., ... & Zhang, C. (2021). Mechanism of the gut microbiota colonization resistance and enteric pathogen infection. *Frontiers in Cellular and Infection Microbiology*, *11*, 716299.

157.Pickard, J. M., Zeng, M. Y., Caruso, R., & Núñez, G. (2017). Gut microbiota: Role in pathogen colonization, immune responses, and inflammatory disease. *Immunological reviews*, 279(1), 70-89.

158.Casadevall, A., & Pirofski, L. A. (2000). Host-pathogen interactions: basic concepts of microbial commensalism, colonization, infection, and disease. *Infection and immunity*, *68*(12), 6511-6518.

159.Lopetuso, L. R., Petito, V., Graziani, C., Schiavoni, E., Paroni Sterbini, F., Poscia, A., ... & Khalil, M. M., Sulaiman, G., Gaballa, M. F., & Attitalla, I. H. Investigation of Bacterial Flora on Mobile Phones: A Comparative Study between Healthcare Workers and Non-Healthcare Workers.

160.Putignani, L., Del Chierico, F., Vernocchi, P., Cicala, M., Cucchiara, S., Dallapiccola, B., & Dysbiotrack Study Group. (2016). Gut microbiota dysbiosis as risk and premorbid factors of IBD and IBS along the childhood– adulthood transition. *Inflammatory bowel diseases*, *22*(2), 487-504.

161.Maharshak, N., Ringel, Y., Katibian, D., Lundqvist, A., Sartor, R. B., Carroll, I. M., & Ringel-Kulka, T. (2018). Fecal and mucosa-associated intestinal microbiota in patients with diarrhea-predominant irritable bowel syndrome. *Digestive diseases and sciences*, *63*, 1890-1899.

162.Vich Vila, A., Imhann, F., Collij, V., Jankipersadsing, S. A., Gurry, T., Mujagic, Z., ... & Weersma, R. K. (2018). Gut microbiota composition and functional changes in inflammatory bowel disease and irritable bowel syndrome. *Science translational medicine*, *10*(472), eaap8914.

163.Bhattarai, Y., Muniz Pedrogo, D. A., & Kashyap, P. C. (2017). Irritable bowel syndrome: a gut microbiotarelated disorder?. *American Journal of Physiology-Gastrointestinal and Liver Physiology*, *312*(1), G52-G62.

164.Casén, C., Vebø, H. C., Sekelja, M., Hegge, F. T., Karlsson, M. K., Ciemniejewska, E., ... & Rudi, K. (2015). Deviations in human gut microbiota: a novel diagnostic test for determining dysbiosis in patients with IBS or IBD. *Alimentary pharmacology & therapeutics*, *42*(1), 71-83.

165.Watson, E., & Reid, G. (2018). Metabolomics as a clinical testing method for the diagnosis of vaginal dysbiosis. *American journal of reproductive immunology*, 80(2), e12979.

166.Khalil, M. M., Gaballa, M. F., Sulaiman, G., & Attitalla, I. H. (2024). Epidemiological Assessment of the Burden and Determinants of Methicillin-Resistant Staphylococcus aureus (MRSA) Infections in Wounds. *Int. J. Bio. & Medic. Science*, 7(05), 39-50.

167.Brüssow, H. (2020). Problems with the concept of gut microbiota dysbiosis. *Microbial biotechnology*, *13*(2), 423-434.

168.Paprotny, Ł., Celejewska, A., Frajberg, M., & Wianowska, D. (2019). Development and validation of GC–MS/MS method useful in diagnosing intestinal dysbiosis. *Journal of Chromatography B*, *1130*, 121822.

169.Parfrey, L. W., Walters, W. A., & Knight, R. (2011). Microbial eukaryotes in the human microbiome: ecology, evolution, and future directions. *Frontiers in microbiology*, *2*, 153.

170.Peixoto, R. S., Harkins, D. M., & Nelson, K. E. (2021). Advances in microbiome research for animal health. *Annual Review of Animal Biosciences*, *9*(1), 289-311.

171.Arcidiacono, S., Soares, J. W., Philip Karl, J., Chrisey, L., Dancy, C. B. C., Goodson, M., ... & Racicot, K. (2018). The current state and future direction of DoD gut microbiome research: a summary of the first DoD gut microbiome informational meeting.

172. Apprill, A. (2017). Marine animal microbiomes: toward understanding host–microbiome interactions in a changing ocean. *Frontiers in Marine Science*, *4*, 222.

173.Kostic, A. D., Howitt, M. R., & Garrett, W. S. (2013). Exploring host-microbiota interactions in animal models and humans. *Genes & development*, 27(7), 701-718.

174.Blaser, M., Bork, P., Fraser, C., Knight, R., & Wang, J. (2013). The microbiome explored: recent insights and future challenges. *Nature Reviews Microbiology*, *11*(3), 213-217.

175.Sanna, S., Kurilshikov, A., van der Graaf, A., Fu, J., & Zhernakova, A. (2022). Challenges and future directions for studying effects of host genetics on the gut microbiome. *Nature genetics*, 54(2), 100-106.

176. Dave, M., Higgins, P. D., Middha, S., & Rioux, K. P. (2012). The human gut microbiome: current knowledge, challenges, and future directions. *Translational Research*, *160*(4), 246-257.

177.Gulliver, E. L., Young, R. B., Chonwerawong, M., D'Adamo, G. L., Thomason, T., Widdop, J. T., ... & Forster, S. C. (2022). the future of microbiome-based therapeutics. *Alimentary Pharmacology & Therapeutics*, 56(2), 192-208.

178.Mahmoud, R., Gaballa, M., Alsadi, I., Saleh, A., Abd Alati, M., & Abid, A. A. (2024). Microbiological Evaluation of Retail Veal Meat in the City of Al Bayda, libya. *AlQalam Journal of Medical and Applied Sciences*, 335-340.

179.Comizzoli, P., Power, M. L., Bornbusch, S. L., & Muletz-Wolz, C. R. (2021). Interactions between reproductive biology and microbiomes in wild animal species. *Animal Microbiome*, *3*(1), 87.

180.Comizzoli, P., Power, M. L., Bornbusch, S. L., & Muletz-Wolz, C. R. (2021). Interactions between reproductive biology and microbiomes in wild animal species. *Animal Microbiome*, *3*(1), 87.

181.Diaz, J., & Reese, A. T. (2021). Possibilities and limits for using the gut microbiome to improve captive animal health. *Animal microbiome*, *3*(1), 89.

182.Sharma, A., Das, P., Buschmann, M., & Gilbert, J. A. (2020). The future of microbiome-based therapeutics in clinical applications. *Clinical Pharmacology & Therapeutics*, *107*(1), 123-128.