THE IMPORTANCE AND RELEVANCE OF OPTIMIZING MICROBIOTA COMPOSITION IN THE TREATMENT OF VARIOUS DISEASES

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Abstract. The deliberate alteration of the microbial community's structure and function, known as microbiota modulation, is a new approach that has the potential to alleviate a plethora of health problems. The underlying concepts of microbiota regulation and its numerous applications to human health, healthcare administration, and pharmaceutical therapies are demonstrated in this review. There is a detailed description of many approaches, including nutritional treatments, fecal microbiota transplantation, antibiotic treatment, bacteriophages, microbiome engineering, and immune system regulation. Trillions of bacteria make up the gut microbiome, which has a significant impact on human health by influencing immunological responses, metabolism, and brain processes. Numerous inflammatory illnesses, metabolic problems, and neurological diseases are linked to disruptions in the composition of the gut microbiome. It is quite challenging to identify the underlying mechanisms and establish cause and effect, though. Preclinical models can uncover new therapeutic approaches and provide important insights into the involvement of the gut microbiota in illnesses. To evaluate the usefulness of preclinical models, such as animal and cell-based models, in clarifying the causative role of the gut microbiome in various diseases, the Human Microbiome Action Consortium launched a Delphi survey. The Delphi survey sought to solve the difficulty of choosing suitable preclinical models to properly explore host-microbiome interactions and examine disease etiology. To get opinions from a wide range of stakeholders, we used an organized method that included expert seminars, a literature review, and the Delphi questionnaire. In order to address the causal relationship between the gut microbiota and disease pathogenesis, experts were asked to assess the models' advantages, disadvantages, and applicability. The resulting suggestions and consensus statements offer important information for choosing preclinical models in upcoming research on disorders linked to the gut microbiota.

Keywords. Immune-mediated illnesses, gastrointestinal disorders, gut microbiota, microbial communities, microbiota regulation, safety concerns, treatment approaches, translational research

Introduction. The diverse and cell-rich community of bacteria that live in the gastrointestinal system is known as the gut microbiota. Due to the microbiota's significant impact on human health and illness, their significance in biomedical research has been acknowledged within the last 20 years. Bacteria, viruses, fungi, and archaea make up the microbiota, a complex ecosystem that interacts dynamically with its host to influence a variety of physiological processes and play a crucial role in preserving homeostasis. Our understanding of the gut microbiota's role in health and disease has been completely transformed by advances in sequencing technology and analytical techniques, which have made it possible to gain important insights into the makeup and function of the microbiota. There is growing evidence that the gut microbiota is intimately related to many facets of human health, from immunological response and metabolic control to behavior and brain development. Changes in the microbiota's diversity, abundance, and composition that are causally linked to the pathophysiology of both acute and chronic illnesses are referred to as dysbiosis [1-5]. A number of host processes, such as

the immunological and neurological systems, metabolism, and intestinal barrier functions, may be impacted by this shift in the microbial population, which may create favorable or unfavorable conditions for pathogens and the commensal microbial milieu. Preclinical models, such as organoids, gut-on-a-chip, and germ-free animal models, have been developed and used more frequently in the last ten years with the goal of more accurately simulating or reflecting physiological conditions. Additionally, these models can determine the underlying mechanisms and establish cause-and-effect relationships within host-microbiome interactions. We evaluated the significance of preclinical models, including the most recent ones, in determining the causal relationship between changes in the gut microbiome3 (i.e., microorganisms and the products of their activities) and diseases, as well as in showcasing the potential of microbiome-derived interventions as therapeutic candidates, using a Delphi survey. The underlying concepts of microbiota regulation and its numerous applications to human health, healthcare administration, and pharmaceutical therapies are demonstrated in this review [6-11]. There is a detailed description of many approaches, including nutritional treatments, fecal microbiota transplantation, antibiotic treatment, bacteriophages, microbiome engineering, and immune system regulation. Clinical applications of microbiota-modulating drugs to immune-mediated illnesses and gastrointestinal disorders demonstrate this therapeutic significance. The study also discusses the difficulties in applying research findings to clinical practice while taking safety into account and offers suggestions for future research directions in this quickly evolving field. Because of its innovative nature in healthcare breakthroughs that enable individuals all over the world to control their diseases, microbiota modification holds a prominent position. Numerous areas of health and medicine are affected by microbiome regulation, including gastrointestinal problems, neurological illnesses, metabolic syndrome, and infectious infections. However, optimizing the potential of microbiota regulation requires a number of strategies to address problems related to standardization, optimization, safety, and supervision. By utilizing its rapid research, incorporating teamwork, and adopting innovative approaches, the science of microbiota modification has the potential to revolutionize healthcare [12-19]. The most significant and recent developments in the understanding of the gut microbiota's involvement in human health and illness are compiled in this overview. The external elements that impact the human microbiome—in this case, the built environment microbiome—are the subject of the first section of our review. The gastrointestinal microbiota's role in the pathophysiology of numerous disorders on numerous axes, including the gut-lung and gut-brain axes, is highlighted in the sections that follow. Lastly, we provide an overview of the new approaches to managing the gut microbiota in the prevention and management of different conditions [20-29].

The main purpose of the presented manuscript is to conduct a brief analysis based on the results of authoritative scientific works regarding the importance and relevance of optimizing microbiota composition in the treatment of various diseases.

Dysbiosis of the human microbiome and microbiota in illnesses. We now have a better understanding of every typical microbial community that exists within the human body because to recent developments in the study of the human microbiome. Thus far, research on microbiota has shown that microbe-host interactions occur not just within an organ but also form an inter-kingdom crosstalk that connects naturally disparate organs. In fact, a great deal of research has been done on the gut microbiota, and it has been demonstrated that it plays a role in the systemic and local regulation of homeostasis in the brain and lungs as well as the gastrointestinal tract. Additionally, through the most significant inter-organ linkages, such as the gut-lung and gut-brain axes, gut dysbiosis contributes to the development of numerous disorders. Human diseases are caused by microbial dysbiosis. Numerous organs, including the heart, brain, liver, kidneys, and lungs, depend on gut flora for proper operation. However, any

disturbance of the homeostasis of the microbiota leads to the dysfunction of these impacted organs and the development of numerous associated illnesses [21-31].

A thorough overview of clinical applications in gastrointestinal illnesses. Since the digestion, absorption, and removal of nutrients are all part of the appropriate function of the gastrointestinal tract—which is arguably the human body's guts—a healthy GI system translates into overall organismic well-being. A wide range of symptoms, from little discomfort to crippling illnesses, are caused by a variety of pathogenic conditions that affect the design and/or function of the digestive tube, such as gastroenterological pathologies. Due to their complicated aetiology or a wide variety of symptoms and behaviors when they react to treatment in individuals, these diseases cause significant clinical issues. In recent years, identifying the pathogenesis, diagnosis, and treatment of gastrointestinal illnesses has yielded about seven pertinent findings. Innovative diagnostic methods, like those related to imaging methods and molecular biomarkers, have made it possible to detect conditions with greater sensitivity and to monitor those conditions, among other things [5-12]. Additionally, methods like targeted biologics and microbiota-based therapies have emerged as a viable strategy for achieving favorable outcomes for refractory disorders. Inflammatory Bowel Diseases (IBD): Crohn's disease and ulcerative colitis, a chronic inflammatory disease type with reversible episodes of intestinal inflammation, are classic male members of the IBD group. Evils like severe morbidity that results in strictures, fistulas, and colorectal malignancies are among these complicated illnesses that entail semantic distortion. Surgery and nutrition are two of the many intervention techniques used in the multidisciplinary treatment of IBD. Recent efforts to treat IBD have mostly focused on administering early and intense therapy that form induction to both reduce corticosteroids and increase completion. The use of biological therapeutics, such as anti-TNF antibodies, in conjunction with immunosuppressive agents that target specific cytokines, such as TNF-α, has revolutionized the treatment of IBDs because these drugs have far fewer harmful side effects and better outcomes than older ones. However, certain patients may develop symptomatology that is extremely resistant to medical treatment; in these circumstances, further evaluation by endoscopic and/or surgical procedures is necessary. Numerous endoscopic techniques, such as radiofrequency ablation (RFA) and endoscopic mucosa resection (EMR), were developed because they offer successful treatment for Barrett's esophagus and early esophageal neoplasia with maintained eradication of the dysplastic tissue without impairing the esophagus's ability to function normally. Furthermore, a number of minimally invasive surgical techniques, such as laparoscopic fundoplication, have demonstrated efficacy in GERD patients who have not responded to pharmacological treatment or who are allergic to long-term PPI use [13-23].

Probiotic and prebiotic effects on the composition of the microbiota. Probiotics, prebiotics, synbiotics, and postbiotics (PPSP) have the potential to prevent metabolic disorders since they are potent regulators of the gut microbiota. Elie Metchnikoff proposed that yoghurt's beneficial bacteria may be used to modify the gut microbiome and improve health. This gave rise to the idea of probiotics in medicine. Probiotics are currently defined as "live strains of strictly selected microorganisms which, when administered in adequate amounts, confer a health benefit on the host." Probiotics are germs that promote the growth of other microbes, according to Lilly and Stillwell. *Lactobacillus, Bifidobacterium* and *Enterococcus* are examples of beneficial bacteria that contribute to the stability of the gut microbiota. The genera *Lactobacillus, Bifidobacterium, Lactococcus, Streptococcus* and *Enterococcus* comprise the majority of human probiotic microbes. Furthermore, certain yeast strains from the family Saccharomyces and Gram-positive bacterial strains from the species Bacillus are frequently utilized in probiotic goods [6-16]. 56 obese women, ages 25 to 45, were split into two groups for the Jagielski et al. study. Group A (n = 31) followed a low-calorie diet (1100–1300 kcal) enriched with probiotic and prebiotic products

(fermented milk drinks, pickled vegetables, groats, lentils, fish oil, highly mineralized water). Group B (n = 25) adhered to a typical diet for weight loss. Both groups reported improved eating habits and comparable decreases in body weight, body fat, and waist circumference after three months. Reducing the amount of calories in the diet, eating regular meals, and consuming more fruits, vegetables, and whole grains—rather than only fermented foods—were the main causes of these improvements.The variations in how the various medication classes affect the microbiome [26-32].

Prospective paths and suggestions. The results of the Delphi poll demonstrate the agreement among professionals in the field and offer significant insights into therapeutic therapies aimed at the gut microbiome. The positive outlook on the therapeutic potential of gut microbiome modulation across a range of disorders is a crucial lesson, highlighting the increasing acceptance of microbiome-targeting therapies as effective methods for treating ailments including obesity, T2DM, and IBD. In particular, for IBD, T2DM, and liver illnesses, experts found a variety of beneficial therapies, such as dietary changes, synthetic consortia, postbiotics, synbiotics, and prebiotics. In particular, dietary interventions were found to be a highly preferred strategy among respondents in all situations examined, suggesting its applicability in therapeutic approaches. On the other hand, the lack of agreement about autism therapies highlights the need for more investigation into the intricacies of the microbiome's function in neurodevelopmental disorders. Notably, there was a negative consensus on the use of antibiotics in the setting of autism, type 2 diabetes, and obesity, indicating the need for alternative therapeutic methods in these areas as well as care in their use [5-11]. The universal agreement that nutrition and lifestyle significantly influence the human gut microbiome, with dietary interventions being the most often accepted therapeutic modulator, is another important theme that surfaced from the survey. In summary, the Delphi survey emphasizes the therapeutic potential of gut microbiome modification while stressing the necessity of exacting procedures and suitable model selection in microbiome research. The optimism surrounding microbiome-targeted therapeutics is reflected in the consensus on promising interventions and future modalities, opening the door for creative methods to managing a variety of disorders. To fully utilize the therapeutic opportunities offered by the gut microbiota and address the problems outlined, researchers, physicians, and industry stakeholders must continue to collaborate. The recommendations derived from the Delphi survey findings are detailed. These provide actionable insights into advancing microbiome research and clinical applications, highlighting the collective expertise and priorities of the contributors [23-31].

Discussion. As humans evolve, so does the gut microbiota. Additionally, it interacts constantly and dynamically with the host's gastrointestinal milieu, making it susceptible to numerous endogenous and exogenous influences. The BE microbiome is one of the latter, and it can significantly affect human health. After numerous impressive and enormous efforts, we are positive that the gut microbiota establishes a multidirectional crosstalk with the host organs involved in maintaining global homeostasis. These flora-organ interactions are now referred to as the gut-lung, gut-brain, gut-skin axis, and many more due to recent scientific advancements in this subject. One of the primary risk factors in the pathophysiology of numerous diseases, such as gastrointestinal tract inflammation, metabolic and cardiovascular-renal problems, and neurological disorders, is any change in these axis in terms of microbial dysbiosis. A significant advancement is made in this regard that allows us to consider targeting the gut microbiota as a treatment more thoroughly, even if we still only have a basic understanding of all the underlying mechanisms in such illnesses [3-11]. The diversity modification in the microbial intestinal community that causes the beginning or aggravation of many diseases still needs to be better understood, despite breakthroughs in molecular biology and sequencing technology. In order to prevent such illnesses, new screening or diagnostic methods could be created to more accurately target the population at high

risk. Targeting particular microbial components or metabolites in a therapeutic setting may be useful in treating a variety of illnesses. Other approaches, such the FMT, metabolites, phages, and miRNAs, are being clinically investigated in addition to the pre- or probiotics, which are the conventional and first choice of microbial therapeutics. However, the application of the aforementioned techniques in the modification of gut microbiota is hampered by numerous limitations in the preclinical and clinical findings. Therefore, additional research in this area is needed to better understand the factors that need to be taken into account while treating patients with these approaches. Targeting the microbiota creates a new therapeutic window for many significant metabolic and neurological illnesses, despite all the current limits and differences. Because it gives many patients hope, it needs more study focus. Microbiota will be the source of the medicine of the future [14-21]. Finding delicate and secure ways to address microbial dysbiosis in order to prevent and treat numerous illnesses is, nevertheless, a major issue. The innovative technique of microbiota manipulation has profound implications for human health and the treatment of illness. The methods outlined in this paper show promise for treating a variety of immunologically mediated illnesses, controlling gastrointestinal issues, and modifying immune responses. Even though there are still issues like standardization and clinical translation, ongoing research will shed light on the intricate processes and enhance the future therapeutic effectiveness of microbiota-modulating drugs. The significance of microbiota modification in altering treatment paradigms and advancing personalized medicine is emphasized in this study [23-32].

Conclusions. The development of obesity is increasingly associated with problems of the intestinal microbiota, which plays a significant role in the regulation of metabolic, immunological, and hormonal processes. Among other factors, overweight people have a lower genus diversity of the microbiota and a higher ratio of Firmicutes to Bacteroidetes. There is a lot of evidence indicating dysbiosis and obesity are related, but it's unclear which way this association goes—obesity may possibly have an impact on the microbiota's makeup. Interventions that alter the microbiota, such as the use of probiotics, prebiotics, dietary modifications, exercise, or faecal microbiota transplantation (FMT), seem to be promising therapeutic approaches. To evaluate their effectiveness and safety, more clinical trials are necessary. A better knowledge of how the microbiota and metabolism interact could help create more individualized and efficient obesity treatments.

We have gradually discovered a new role for bacteria in health and illness after decades of investigation. It is now established that nearly every element of the host can be impacted by microbiota, and that a wide range of illnesses are linked to its dysbiosis. We can now closely examine how bacteria contribute to pathogenesis and preserve human health thanks to cutting-edge research methods. However, the bacterial component of microbiota is the primary focus of research; the significance of viruses, fungi, and other microorganisms in health and illness is still mostly unclear. Furthermore, whereas microbial dysbiosis is frequently seen in illness conditions, the microbiota's causal involvement is yet unknown. As a result, there are still many unanswered questions in this area. The development of microbiota-based treatments like FMT and bacterial modulation has been made possible by a better knowledge of the host-microbiota interaction. When it comes to treating conditions like diabetes, inflammatory bowel disease, C. difficile infection, etc., these approaches are well on their way to attaining the best possible therapeutic outcome. In conclusion, by manipulating the microbial symbionts, we are now better equipped to cure illnesses and promote health.

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