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The Impact of Microbiome on Human Health and Disease

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ABSTRACT

An intricate and ever-changing assemblage of microbes inhabiting different regions of the human body, known as the human microbiome, is essential for preserving human health and exerting an impact on disease processes. This review examines the configuration, roles, and physiological interactions of the microbiome, especially in the gastrointestinal tract, and emphasises its substantial influence on the immune system, metabolic activities, and pathological conditions. Furthermore, we investigate the notion of dysbiosis, which is the association between changes in the makeup of the microbiome and diseases such as colorectal cancer, diabetes, and neurological problems. The review elaborates on existing approaches for investigating the microbiome, therapeutic treatments aimed at microbiota such as probiotics, prebiotics, and faecal microbiota transplantation, and their promise in the treatment of disorders linked to microbiome dysregulation. Elucidating the function of the microbiome in health and illness provides new perspectives on the preventive and treatment approaches for diseases.

Keywords: Human Microbiome, Gut Microbiota, Dysbiosis, Immune System, Microbiome and Disease.

INTRODUCTION

The human microbiome consists of the complete set of microorganisms, and their genes, that live in different parts of the human body, including the skin, nose, mouth, gut, lungs, and urogenital tract. The term "microbiota" is often used interchangeably with the term "microbiome," but strictly speaking, "microbiota" refers to the community of microorganisms inhabiting a body site, and "microbiome" refers to the genetic and biochemical information of that microbiota. Like the Earth's ecosystems, our bodies host a variety of different microbiomes, each featuring unique sets of microorganisms with different functions. Most studies have focused on the gut microbiome because it is the most diverse and has the strongest connection to the health of an individual. In recent years, research using large-scale sequencing technologies has begun to uncover the numerous roles these millions of tiny inhabitants play in human health and disease [1]. The human body consists of about 37 trillion cells, but it is also host to an estimated 100 trillion bacteria, fungi, viruses, and other microorganisms that reside in and on our bodies. By some estimates, a person's microbiota can weigh as much as four and a half pounds. These communities of microorganisms produce chemicals, communicate with human cells, aid in digestion and vitamin synthesis, contribute to nutrient absorption, prime the body's immune system, and help protect the body from disease-carrying bacteria. The human microbiome contains about 20,000 different distinct and identified protein-coding gene families for comparison. By contrast, the human genome contains just 20,000 to 25,000 protein-coding gene families [2].

DEFINITION AND COMPOSITION

A microbiome is defined as the entire genetic complement of a community of microorganisms. The human microbiome is a complex and diverse entity, viewed as a dynamic collection of microorganisms, including viruses, bacteria, fungi, and archaea, and their genetic material as well as host cells should be considered. This population represents a similar number of host and bacterial cells, with an equilibrated equilibrium

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regulating the entire ecosystem. Moreover, several recent studies describe the development of the neonatal gut microbiome and how it establishes itself over time. They argue between two initial methodological approaches: some argue that the fetus is sterile due to the inaccessibility of the uterus compared to the vagina; others argue that every human being has a little indigenous brigade throughout life, due to some special locations inherent in biology [3].

The microbial composition in the human body varies between different locations in the body with the highest load of microorganisms present in the large intestine, contributing 95% of the entire human microbiome and including over one thousand different species. The human microbiome can be a positive ally for human health by contributing to the health of several systems. The healthy indigenous microorganisms of the skin, mouth, genitals, and intestine fully serve the body in several ways: first, local beneficial bacteria protect against other hostile/threatening microorganisms that try to enter through the body opening; second, beneficial microorganisms stimulate the immune system to produce buffed-white blood cells, which inactivate harmful microorganisms; third, digestion, energy, and vitamins are supplemented/provided by the various microorganisms during the breakdown of beneficial and resveratrol microorganisms [4].

ROLE IN HUMAN PHYSIOLOGY

The human body and the human microbiome have a mutualistic relationship. The gut microbiome is vital to digestion, nutrition absorption, and the development of the immune system. It also produces beneficial molecules that the human body cannot, such as metabolites and vitamins. The gut microbiota is involved in drug metabolism and the initiation and progression of metabolic, neurological, and developmental diseases. Germ-free animals have shown the roles of the gut microbiome in host physiology. Disease associations annotated include colorectal cancer, irritable bowel syndrome, metabolic syndrome, diabetes, and antibiotic resistance [5].

METHODS OF STUDYING THE HUMAN MICROBIOME

Human microbiome is the aggregation of microbes inhabiting the human body. Its contribution to human health is now widely acknowledged, with alterations to the microbiome associated with several human diseases. Investigations aiming to characterize the human microbiome, and to decipher its implications, have become increasingly pervasive both from a research and from a clinical perspective. Several techniques have been employed to study the microbiome, which has contributed to our understanding of the complexities of microbiomes in different populations and under several pathological states. Both DNA and RNA can be targeted by sequencing techniques to gain insight into microbial population structure, function and gene expression. Furthermore, this can be performed for all the residing microbiota (host plus microbial DNA) or specifically on one kingdom of life (e.g. bacteria, fungi, or viruses) [6]. Comprehensive studies that have characterized the human microbiome using DNA extraction include the Human Microbiome Project (HMP), MetaHit and the recently published Flemish Gut Flora Project. Differences in sampling methods (e.g. the different body sites sampled), DNA amplification (targeting different variable regions of the 16S rRNA gene), sequencing technology, bioinformatics analysis and statistic interpretation (Simpson/invsimpson, unweighted or weighted unifrac) prevented successful integration of results. More recently, studies have begun to focus on RNA extraction methods in order to understand the functional characteristics of the microbiota and the functional products of microbial communities rather than taxonomic profiles. Microbial gene expression in the large intestine or of the fecal microbiota has been able to capture microbial metabolic changes in response to dietary intervention, colonization of gnotobiotic mice, or IBD (amongst others) potentially more sensitively than 16S rRNA gene profiling. This overview will discuss some of the approaches used to study the microbial community, identifying the advantages and pitfalls of each as well as the need for complementary methods [7].

MICROBIOME AND IMMUNE SYSTEM INTERACTIONS

It is hard to underestimate the importance of the interaction between the microbiome and the immune system. There is an established fact that most of the immune system is related in one way or another to detect or eradicate microorganisms or their products. The number of different cell or tissue types involved in immune responses to microbes with very fine-tuned complexities. Conversely, the immune system - by controlling the resident microbes and preventing the invasion of pathogens - regulates many of the immune responses to food, commensals, etc., belonging to the large category collectively known as antigens located in the lumen of the gastrointestinal (GI) tract. The term used to describe these interactions is coined tightly regulated. If one party fails to obey the regulatory effect of the other, infection and/or pathology ensue [8]. In some communities, quite a large proportion of the immune system is dedicated to making the microbiota invisible to the host or to attenuate local and systemic

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immune responses to resident microbes. Inflammation and basal-like immune cell integrative functions of tissues can occur when such immunoregulatory mechanisms are compromised. The presence in the human body of between 10 and 100 trillion cells is estimated to be 10% epithelial and 90 percent non-epithelial, with the latter amount including many different commensal microbes and their collective genes, which altogether make up the microbiota. Having coevolved with its host over billions of years, the microbiota seems - however - to be more flexible to disturbance and rapid restoration to near normal (eubiotic) states than might be expected [9].

DYSBIOSIS AND DISEASE

Dysbiosis, a term used to describe shifts in the community structures of the microbiota and correlated changes in the host's homeostasis, has been associated with a variety of human diseases. It is important to point out that the mere presence of an altered microbiota does not necessarily implicate a causal role in the disease development or progression. For instance, the early detection of similarities between the differently structured intestinal microbiota communities in patients suffering from Alzheimer's disease, neurodevelopmental disorders, and other brain-related illnesses has been interpreted as a further indication of gut-centric symptomatology and impaired gut-brain communication. Dysbiosis of the gut microbiota has likewise been correlated with other local disturbances and pathology, including colorectal cancer [10]. Although these associations may sometimes provide a rationale for a causal link, much more evidence, leveraging knowledge from animal models, genomics, metagenomics, and mechanistic science, is needed. Disruptions of microbiome homeostasis have been categorized into three main types of dysbiosis: loss of microbial community redundancy, reduced phylogenetic diversity, and shifts in the compositional structure of the microbiome. Each type of dysbiosis has been associated with human health. Importantly, considerable evidence now supports and specifies the causality of some microbe-disease associations and the contribution of disturbed microbial community structures to human health [11-14].

THERAPEUTIC INTERVENTIONS TARGETING THE MICROBIOME

Given the increasing understanding of the composition of the human microbiota and their influence on wellbeing and disease, there have been considerable efforts investigating strategies to modulate the microbiome. Microbiota-targeted therapeutic interventions can employ various well-points. At present, re-establishing dysbiotic states with selected probiotics or fecal microbiota transplantation is at the forefront of clinical efforts. A major difficulty for functional investigations of the human microbiome is linked to its diversity among healthy individuals. This is true not only for the composition of the microbiota but also for its associated functions and metabolic activities [12]. Microbiota-directed therapeutic strategies and treatments may arise from synthetic microbiota design, dietary supplements, prebiotics, probiotics, fecal microbiota transplantation, phage therapies, and flavonoid therapy. Prebiotics are defined by a "substrate that is selectively utilized by host microorganisms conferring health benefit". Some known targets are nucleosides, peptidoglycan sugar backbone, l-alanine, l-lysine, l-valine, l-leucine and d-lactate, but it is not only in regards to specific sugars to be utilized, i.e., influencing the production of short chain fatty acids, as fructo-oligosaccharides and β-glucans have anti-inflammatory properties and arabinogalactans can regulate host stress responses. There are differing opinions on prebiotics and their use, with some researchers expressing skepticism when prebiotics are included as a commensal garden-in-a-pack with additional microbes in the form of a probiotic, as the effect of the "added" microbes cannot be determined. However, the scientific literature has identified prebiotic ingredients with significant benefits in treating a variety of disorders when administered alone or in combination with a probiotic product [13,14].

CONCLUSION

The human microbiome, particularly the gut microbiota, is integral to numerous physiological processes, including digestion, nutrient absorption, immune system regulation, and the prevention of pathogen invasion. Dysbiosis, or the disruption of the microbiome's balance, is increasingly linked to a variety of diseases, from metabolic disorders to neurological conditions. Advances in sequencing technologies and microbiome research have illuminated the complex interactions between the microbiome and the human host, offering promising avenues for therapeutic interventions. Future research should focus on the development of personalized microbiome-based treatments and a deeper understanding of the microbiome's role in disease etiology, paving the way for novel preventative and therapeutic strategies in medicine.

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