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The Role of Gut Microbiota in Human Health and Disease

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Abstract: The human gut microbiome is the focus of intensifying scientific investigations. Several large-scale projects have been initiated, including but not limited to the Western simplifying Human Microbiome Project (HMP) and the European Union Metagenomics of the Human Intestinal Tract (MetaHIT). These large-scale endeavors both share similar missions in characterizing the human microbiome and their roles in health and disease states, with MetaHIT solely focusing on the gut microbiome. There are several analyses have been incorporated in these meta-omics projects including (1) 16S ribosomal RNA (rRNA) sequencing to taxonomically characterize the microbiota communities (2) Whole Genome Shotgun (WGS) metagenomic sequencing of body-site specific whole community DNA, followed by reference genome mapping,

metagenomic assembly, gene cataloging and metabolic reconstruction, to facilitate maximal capture of organismal and functional data of the human microbiota. Due to the inherent complexity and heterogeneity of the human microbiome, several experimental models have been launched (all following the Western simplifying HMP criteria) where gnotobiotic animals are colonized with simplified, known consortium of bacterial strains (a model of the human microbiome). These new "simpler" model animals will prospectively exhibit divergent health conditions (ranging from obese to metabolic syndrome to IBD), illustrating the causation links between particular microbiota community members or gene functions and these health silences. This knowledge is expected to open up new avenues for future therapeutic approaches for reshaping an ensemble of human associated microbial communities and their genetic functions to confer or restore good health [1]. The symbiotic relationship between the gut microbiota and the host is regulated and stabilized by a complex network of interactions that encompass metabolic, immune, and neuroendocrine crosstalk between them, and it has been proposed to physiologically link the gut with several health conditions, including the CNS, the immune system, and the endocrine system. Chronic diseases such as obesity, metabolic syndrome, mood disorders, and immunological dysregulations are postulated to at least in part derive from bi-direction aberrant communication routes between the GIT and these organs due to

conditions such as high fat diet, chronic psychological stress, infection, or chronic use of antibiotics. These conditions can potentially alter the complex mutually beneficial relationship between the gut microbiota and the host, resulting in disturbances of the microbial population and the possible occurrence of dysbiotic health conditions.

Keywords: Gut microbiota, microbiome, health, disease, gut-brain axis, probiotics, and metabolic syndrome.

1. Introduction

The human gastrointestinal (GI) tract represents one of the largest exposed surfaces in the human body. The number of bacteria within it is greater than the total number of human cells in the body. The gut microbiota plays a central role in a healthy individual's overall health. An increase in interest and subsequent research regarding the importance of the gut microbiota in human health is currently underway. In view of increasing interest in this research area, the gut microbiota's potential role in a variety of health conditions must be critically examined. What are the current gaps in fully understanding the gut microbiota's effect on the human body in healthy, diseased, or transient disease states? Why is it difficult to learn the potential far-reaching health implications of gut microbiota? Applications to the public health community and medical community will be discussed, recent research regarding gut microbiota composition and its association with general health and disease implications, and future perspectives for research. [2][3][4]

Literature Review

2. Historical Perspective on Gut Microbiota Research

The exploration of the microorganisms residing within the human gastrointestinal tract has a history as long as microbiological science itself. Antony van Leeuwenhoek was the first person to have directly observed and sketched bacteria, which he found in the human mouth, and some fabricated from a fecal sample of his own in the late 1600s. He also surmised that the microorganisms in human excrement may vary. Observations of microbes in the healthy rectum were made by Binaghi in Italy, and Iwan Bersenius in Germany during the mid-1800s. Further studies of the gut ecosystem and microbiota were carried out by Theodor Escherich in the next years. A culture-independent analysis of the stool specimen from Typhoid patients was described by Julius Petri and Walther Hesse in 1887. The idea that humans might not be a single organism but rather a superorganism harboring immense numbers of microorganisms led the way for Sidney Finegold and Martin J. Sutter in the re-discovery of the role of sulfite-reducing clostridia in health and disease [5]. It had previously been thought that all bacteria of the large bowel of normal humans could be grown and identified using available aerobe-based technologies. Peter Greenberg and Bassler grew Vibrio fischeri in the laboratory, a development that significantly advanced the fields of biochemistry, genetics and study in the microbiology of the gut in a natural role to the bio-illumination system of the Hawaiian bobtail squid.

Materials and Methods

3. Composition and Diversity of Gut Microbiota

The complex community of microbiota resolves as a stark differentiation and “core” group of dramatic and very individual community members, accompanied by a plethora of very variable ones. The community itself consists of bacteria, viruses, fungi, and archaea. This very broad claim is based on the analysis of the guts of ~1000 people, and so far no other study has been able to contradict it using a similar sampling regime [6]. Unfortunately, the suggestion that everyone’s microbiota conform to one of three equally populated enterotypes has caused much confusion and far less helpful discussion. In reality, this is a very complex and dynamic topic, dependent on a great number of variables including genetics, diet, and any number of other environmental factors. Each microorganism present in the gut microbiota plays a part in shaping this community.

The gut microbiota is a diverse microbial community types consisting of bacteria, viruses, fungi, and archaea. Every individual has its unique gut microbiota composition, and the relative abundances of its constituent microbial taxa are of random nature. The vast majority of enterotypes pervades the questions of the taxonomy of the gut microbiota and the scope of interindividual variability of the gut microbiota composition. Analyses of the large cohort enabled far more reliable estimation of the scope of the individuality of the gut microbiota and resolved the former spurious findings. Gut microbiota analyses are of a complex and multidimensional nature, and caution is needed in result interpretation. Highly diverse outcomes depend on the physico-chemical method used and the algorithm used in result processing. In a broad view the vast majority of the enterotypes do not exist, the notion on enterotypes per se is of limited applicability, and akin concepts should be abandoned in favor of a common coordinated effort to crack the complex and vital issue of the taxonomy of the gut microbiota. Total microbial genomes exceed the human genome by at least two orders of magnitude and are unprecedentedly diverse, an unmatched wealth of genetic traits. Transferred genes are capable of function in the gut and are expressed there. The vast majority of metagenomic information is unannotated, and this wealth needs to be developed for the benefit of biomedical research. For the vast array of genetic Modi and associates of the gut microbiota the current omic technologies and knowledge base have very limited utility, and there is a long way ahead in order to fathom the complex issues of the diet-microbiota actions and the effects of the diet on the gut microbiota [7]. This daunting challenge is of eminent importance concerning the progressing scourge of metabolic and neurological disorders in the developed world.

Results and Discussion

4. Functions of Gut Microbiota

The human body is teeming with trillions of microbes, outnumbering human cells by a factor of 10. Most of them are found in the gut: it is there that we find a unique ecosystem of bacteria, archaea, eukaryotic microbes, fungi and viruses. Although recent research has been uncovering advances in the field, knowledge about the functions of the gut microbiota is still limited. There are over 500 different species of bacteria in the gut and their functions are very complicated with interdependence, so individual functions are not well understood. Most of the species contained in the gut are not yet culturable, which adds to the difficulty of understanding these extremely complex systems. Despite these difficulties, the main functions of the gut microbiota in the human body are understood. They are: digestion and absorption of nutrients; synthesis of essential vitamins and bioactive compounds; regulation of energy balance between host and microbiota, maintenance of the intestinal barrier, and modulation of immune responses; prevention of the colonization of pathogenic bacteria [8]. The multidimensional importance of the gut microbiota in maintaining human health is increasingly clear and the medical consequences of disruptions in this complex ecosystem are being more and more widely studied. With a growing effect of 21st-century diseases, it is important that there is a greater understanding of what characterizes health and disease in this complex ecosystem.

5. Impact of Gut Microbiota on Digestive Health

The gut microbiota plays a significant role in gastro-intestinal health, preventing the development of gastrointestinal disorders and sustaining intestinal integrity. The gut microbiota aids in nourishing the intestinal mucosa, making it impervious to unfriendly microorganisms, antigens, and pathogens. The microbiota is instrumental in fostering the intestinal barrier by sustaining gut health and the integrity of this function. It aids in the tightening of the links between gut epithelial cells, boosting the mucus layer in the intestine, and supporting the immune system. The interplay between the immune system and the microbiota is seen as a major factor in preventing the onset of gastrointestinal diseases. The Faecalibacterium prausnitzii bacterium generates a huge portion of the butyrate necessary for the colonocytes. The absence of F. prausnitzii can lead to a shortage of butyrate, which is implicated in inflammatory bowel disease (IBD) and bowel cancer. Dysbiosis resulting from the loss of F. prausnitzii triggers irritation and inflammation of the gut, and it can lead to the onset of digestive disorders, such as colitis, Crohn's disease, and irritable bowel syndrome (IBS). Gastroenteritis can also be caused by the either excessive growth or the toxins produced by Clostridium difficile, leading to an imbalance in the gut flora. The gut microbiota can be rendered destructive by many elements, including a high-fat diet or numerous anti-infective drugs. If vitality can be restored to the gut microflora leakage issue, the gut health status can be repaired, and gastrointestinal disorders can be avoided [9]. Inflammatory bowel disease (IBD) is marked by gut microbial arrangements that are distinctly different from the flourishing gut flora. For the prevention and healing of IBD, new therapeutic schemes using antibiotics or faecal microbial transplants have been examined, making it important to regularly test the intestinal microflora.

6. Influence of Gut Microbiota on Immune System

The gastrointestinal tract harbors a large population of commensal bacteria, termed as the gut microbiota, that present a wide variety of species and have an ongoing effect on the health of their host. Growing evidence shows a crucial role of the gut microbiota in the development and functionality of the immune system. This interaction is highly complex and begins at the very first exposure of the human body to microbiota during early life. The innate immune system responds during the earliest encounters with changes in the predominance of different bacterial genera. This crosstalk is crucial for programming proper innate immune cell development, and its disturbance is associated with later life immune abnormalities [10]. The balance of gut bacteria can control the immune responses to systemic infections and the resulting inflammation, which is connected to the relative levels of different bacterial phyla. A very rare inflammatory condition known as linotherapy or IgE-mediated resistance has been shown to occur after systemic exposure to a specific subset of gut bacteria. Overly hygienic conditions should be avoided as they compromise the body's ability to control the immune responses to pathogens.

A representative change in relative abundance of Bacteroidetes and Firmicutes in the gut of nine specific pathogen free mice after colonization with a complex bacterial community from the cecum of regular mice. D is the colonization day. The result of this treatment is a heightened resistance to TH2 immune responses and attenuated infection by pathogenic nematodes. Moreover, resistances to gut bacteria also affect the potency of subsequent infections with other pathogens. Expression of an antimicrobial enzyme and changes in the intestinal niche where bacteria usually develop are vital, serving to regulate the densities of commensal bacteria and preventing the colonization of niche space usually occupied by opportunist infective bacteria. Repeated exposure to heat shock also has deleterious effects on immune cells. Together, these effects can influence the choice of colonizing bacteria and the resulting shaping of the adult gut microbiota. Disruption of this process could have far-reaching consequences for human health. [11][12][13]

7. Gut Microbiota and Metabolic Health

The human gut is colonized by trillions of bacteria that form a complex, highly individualized

community, representing a potent metabolic organ. Gut microbiota is involved in multiple nutrient and drug metabolism pathways and plays a role in the regulation of hormone and bile acid metabolism. During the last 20 years, awareness has grown that gut microbiota has an active role in maintaining host health and can impact major chronic diseases.

A significant body of preclinical data reports association between gut dysbiosis, i.e., alteration of microbiota composition or function, and a variety of disorders, ranging from infectious and inflammatory bowel diseases, to metabolic and neurodegenerative pathologies. The interplay between microbiota and metabolic health has attracted the most attention. For example, gut microbiota has been found to modulate the development of metabolic disorders through several mechanisms, such as enhanced energy extraction from diet and better regulation of fatty acids and cholesterol metabolism. In this vein, there is increasing evidence, in both animal and in vitro models, that certain gut bacteria are able to prevent or ameliorate the onset of metabolic disorders by protecting from diet-induced obesity or diabetes. Several human studies have reported patients with metabolic diseases to have a less diverse microbiota and this metagenomic repertoire has a strong correlation with metabolic outcomes as well. Furthermore, experimental work has highlighted that certain diet regimens can induce changes in gut microbiota composition that are paralleled by metabolic improvements. For example, a high-fat/low-fiber diet in mice results in decreased microbiota diversity, accordingly with metabolic impairments, as compared to microbiota richness increase observed in calorie restriction regimens. Conversely, turn from unbalanced to balanced diet is frequently associated with microbiota compositional changes paralleled by apparent compound beneficial effects on host metabolism. In a study carried out on independent cohorts of patients affected by metabolic diseases, insulin sensitivity and fat storage were found to positively correlate with the gut abundance of several bacterial markers, thus unveiling a microbiota profile to leverage clinically to monitor and predict the metabolic improvement of subjects. Dietary regimens may be conceived to influence the gut microbial community by favoring or inhibiting the growth of specific taxa, thus representing a tool to be exploited for metabolic health purposes. [14][15][16]

8. Gut-Brain Axis: Communication between Gut Microbiota and Brain

The intense attention paid to the gut microbiota has increased over the last several years, driven by growing understanding of its essential role in maintaining overall health. A novel area of microbiota research, the gut-brain axis is attracting increasing interest. It refers to bidirectional communication between the enteric nervous system of the gastrointestinal tract and the central nervous system, facilitating exchanges of bioactive molecules and impulses. Mechanisms allowing communication between gut microbiota and the brain have been identified, demonstrating that both the gut microbiota and the brain can influence each other through neural, endocrine, immune, and humoral pathways. A variety of methods have been adopted to explore the effects of gut microbiota on the gut-brain axis and neurological functions, such as germ-free animal models, probiotics, antibiotics, and infection studies [17]. Over recent years, studies have focused on the effects of depression and anxiety on gut microbiota; a stronger relationship between them is evidenced. Similarly, compelling data for the effects of the gut microbiota on diseases such as anxiety, depression, and neurodegenerative disorders have been frequently reported. Broadly, more and more attention is being given to the gut-brain connection in different cases. In the current review, the recent research important insights into this intricate network. There is now strong evidence that the gut microbiota can affect behavior and cognition while modifying brain physiology [18]. This has shifted the understanding of the microbiota as more than a simple metabolic organ. The focus of the field is beginning to include the possibilities for therapeutic strategies that target the gut-brain connection. A better understanding of this complex axis is critical, providing new strategies to reduce the incidence or progression of neurological diseases. An overview of the current research trends and potential future directions is presented. Finally, it is worth highlighting how profoundly microbiota can affect neurological health. Amplifying insights into the relationship between the gut microbiota and the brain will likely lead to

transformational progress in neurological science. This manuscript is intended to convey the elemental insights on this topic.

9. Dysbiosis: Imbalance in Gut Microbiota

Dysbiosis refers to an imbalance in gut microbiota composition, either as decreased diversity or as alterations in the relative abundance of individual species [19]. A wide range of factors conspire against our invisible allies, ranging from our high-sugar, high-fat, low-fiber diet, to our sedentary, hygiene-obsessed lifestyle, to our frequent, often indiscriminate use of antibiotics. This matters because gut microbes are involved in digesting our food, protecting against infections, educating our immune system and, as has been widely and often sensationally reported as of late, impact the development and severity of a variety of diseases, from metabolic conditions like obesity, to inflammatory bowel disease or cardiovascular conditions [20].

“Dysbiosis in general is thought to reflect a disturbed ecological balance in the gut.” Healthy intestinal flora benefits the host through either its physiologic, metabolic, or immunologic effect. The goodness of the gut microbiota lies in its capacity for protection, colonization resistance, nutrient harvest and energy extraction, and non-nutritional functions like metabolic enzymes production, drug metabolism, or the regulation of intestinal motility and gut hormone synthesis. A dysfunctional gut microbiota, in contrast, correlates with a variety of disorders, from abnormalities in host development and metabolic disorders, including obesity and liver steatosis, to the development of cardiovascular, neurological or behavior abnormalities, and from infection or inflammation to intestinal carcinogenesis, mainly due to its abilities to instigate chronic inflammation, promote the immune alterations of the host, or induce DNA damage. Bloody stool, loss of appetite, constipation for more than 3 weeks with weight loss and fatigue, severe diarrhea for more than 6 times a day are signs that show you have dysbiosis.

10. Factors Influencing Gut Microbiota Composition

The human intestines are colonized by a complex microbial community consisting of many microbiota, their genes and metabolic products, known as gut microbiota. Dietary choice is the most effective way to modulate gut microbiota. The large intestine is the major site of the gut microbiota. The number of microbiota in the large intestine is about 10^14, which is 10 times higher than the number of cells in the human body [21]. The total number of genes of gut microbiota is about 100-fold more than human genes [6]. The gut microbiota’s composition and relative abundance vary among individuals. The composition of the gut microbiota is influenced by intrinsic (e.g., host genetics, age) and extrinsic factors including diet, lifestyle, medications such as antibiotics, and other environmental variables comprising hygienic conditions.

The first influences on gut microbiota discussed are host genetics and age, explaining the intrinsic factors. Heritability of the microbiota is estimated about half 8%; genetic variations have been reported to affect the composition of the gut microbiota. In a twin study, it was discovered that the host’s genetics contribute substantially to the assortment of gut microbiota by 17%, and the interaction between the genetic tendency of the host and environmental aspects plays a role in the selected gut microbiota. Age represents another intrinsic factor affecting microbiota due to changes in the immune system, gut mucosa, and diet. Both the composition of the gut microbiota and its metabolic activity change until the infant reaches the status of an adult. On the other hand, collect the extrinsic factors related to lifestyle, diet, and medications can cause unintended and usually temporary interpersonal variability in the microbiota composition. Since these factors can change frequently, they have a considerable effect on shaping an individual’s microbiota profile. Another point is that the microbiota in one community may vary considerably from another due to the location and different cultural and dietary practices. These results are in line with the frequent alteration of the gut microbiota structure with community changes related to geographic and dietary behavior. From a medical and therapeutic point of view, this understanding could be essential to decide the closest to a healthy community, or to estimate how hard it is for a corrupted community to shift a potentially favorable status. This could help in the future with the

deployment of dietary regimens optimized given the individual's microbiota status, aiming at a precision treatment against, among other things, neurodevelopmental diseases. In general, lifestyle factors have more transient effects on the microbiota compared with host-related factors, such as genetics and as shown by previous studies, individual-specific lifestyle factors have different effects on the change in the composition of the microbiota. Regarding diet intervention, it needs to consider the current state of an individual's microbiota and may focus on the use of diet as a primary treatment for captured imbalances. Overall, an individual-based tailored approach would be the most suitable approach to identifying and reversing obstructions. Although with a substantial impact on the microbiota, diet is unpredictable, leading to the fascinating implications of future research in view of the importance of promoting personalized medicine. The role of gut microbiota in the context of human health and sickness is today a mainstream research topic with broad implications due to the recognized complexity and host-interaction networks. The field of microbiota and host-microbiota interactions are seen as a core issue and feature worldwide in various research, clinical, and industrial strategic visions with potential future and societal implications. Contrary to previously held thoughts, the gut microbiota is turning out to play a crucial and paramount role in various aspects of human health, affecting disorders far beyond metabolic and gastrointestinal diseases. So far, it has been suggested that this is due to several endogenous and exogenous factors capable of shaping the gut microbiota in adolescence and during fundamental life. However, while these insights are relevant and of utmost importance in clinical applications and therapeutic discovery, polymenorrhea considering the dynamic nature of microbiota affected by different life stages and exposures will need to be further understood. Efforts will require sophisticated experimental designs and innovative analytical methodologies that are up to the challenge of untangling the intricate and multifaceted bacterial-host interface. Efforts cannot focus on the gut microbiota only, as the entire human microbiota interface is shaped and partly understood. [22][23][24]

11. Methods for Studying Gut Microbiota

Introduction to the methodology section, explains how the knowledge of gut microbiota can be approached. Presents traditional culture-based methods and modern molecular techniques like metagenomics. Emphasis is on the progress of community-wide understanding including strengths and weaknesses of sequencing-based methods. Application of methods in the human gut microbiota research are discussed along with the tools used for processing samples and giving higher level insights. Provides thought for studying the colonization, colonization resistance and aging of the gastrointestinal microbiome and how time can be influential with this application. Highlights the importance of method selection in the context of understanding the gut microbiota and how modern molecular techniques are on the verge of an explosion in microbiota studies due to high-throughput sequencing technologies. Outlines 1) how such studies have been and currently are applied to research in the gut microbiota, from its association with diseases to its assembly; and 2) the tools and approaches used to collect samples, process libraries, and make sense of the generated data. Ultimately, methods how to address the functional role of the gut microbiota are considered, reflecting a focused growth in viewing health and disease in the digestive tract through the lens of the interacting microbial community and its metabolites.

Microorganisms taken up into the gastrointestinal tract are in continuous contact with its lumen and membrane separating them from the host. As a result, an intricate and complex bacterial community is maintained and there is reciprocal influence exerted between gut microbiota and the host. Normal gastrointestinal microbial communities are known to be important in health but can contribute to the development of many diseases if disrupted. Moreover, the gut is a major entrance for potential pathogens. A basic knowledge of both culture-based normal and pathogenic gastrointestinal microbiota will contribute to the prevention and therapy of many gastrointestinal diseases driven by the disturbance of both commensal populations. Furthermore an increase in the average lifespan of today's population emphasizes the need for a deeper understanding of aging. Time of acquisition of the complex bacterial community of the gut and its aging are poorly

understood fields representing a quantifiable gap in the microbial ecology and infectious disease research [25].

12. Therapeutic Potential of Modulating Gut Microbiota

Gut microbiota has a critical role in human health and disease. The microbiota communities can be modulated or manipulated to promote health and prevent disease. Emerging interest focuses on microbiota as the target for health promotion and disease prevention measures. Therapeutic strategies for modulating the microbiome include dietary modifications, probiotics, and prebiotics. The existing evidence suggests some benefit in specific clinical scenarios using fecal microbiota transplantation, particularly for Clostridium difficile colitis, inflammatory bowel disease, and irritable bowel syndrome. Microbiome therapy has arisen as a promising field of research for the treatment of human health-related diseases.

The last decade has witnessed an explosion in high-throughput microbiome research, as advances in sequencing technologies have allowed the microbial composition to be examined at various body sites. During the same period, metabolomics, metatranscriptomics, and metaproteomics have been employed to investigate microbiome-related metabolites. Human microbial communities have been identified in many other diseases and are now the target of therapeutic preclinical and clinical research. Consequently, the human microbiome has become a part of the new paradigm in the understanding of human health and the development of diseases. Beyond this progress, public scientific literacy is confused and fragmented by non-expert practitioners confused and oversimplified explanation of the meaning of the microbiota-based health findings. Thus, a critical, wide, and translational summary of the potential preventive and therapeutic possibilities of gut microbiota modulation, including its limitations, is needed. In the breeding field of microbiota-based health, this focused perspective paper examines these key issues for researchers and clinicians to gain deeper insight into the potential benefits and better design of intervention programs.

13. Probiotics and Prebiotics: Role in Gut Health

There’s a silent organ in your body, you might not know. It weighs about one to two kilograms, with about 10 times more microbial cells than human cells. This is your intestinal microbiota, which helped you digest the food, protects you from disease, and has a profound impact on your health and happiness. The reciprocal relationship of the gut microbiota with the host is a life-long mutual commitment; both aim to be as favourable for each other as possible. The activity of the microbiota is also dependent on host characteristics and environmental factors, such as diet. Read this far, congratulations—your interest in your gut health will deliver a good return.

A newly well-crafted article on the interactions between the human gut microbiome and gut health, mental health, obesity, and the role of probiotics and prebiotics in gut health is ready for you to dive deeper into the complex world of your gut health. This article will introduce you first to the microorganisms residing in your gut, their multiple roles in maintaining gut health, and the complex communication between the gut and brain.

Probiotics are defined as “live microorganisms which when administered in adequate amounts confer a health benefit on the host.” The word prebiotic is derived from Latin, meaning “before life.” A prebiotic is defined as “a substrate and growth-promoting product of beneficial microorganisms that are located in the colon, the nondigestible part of compounds consumed in the daily diet”. From these simple definitions, one can infer that probiotics are beneficial microorganisms that are ingested and present in food and/or supplements, whereas prebiotics are dietary fibers that support the beneficial microorganisms, promoting their growth and metabolic activity. Prebiotics come mainly in the form of carbohydrate fibers that are relatively simple to design and, hence, provide possibilities for systematic evaluations of the mechanisms by which specific components of the diet can affect gut microbiota dynamics [26].

14. Fecal Microbiota Transplantation (FMT)

Fecal microbiota transplantation (FMT) involves the transfer of donor feces and is emerging as an intriguing therapeutic approach. Several clinical studies have indicated its effectiveness in curing different diseases such as recurrent Clostridium difficile infection (rCDI) [27]. Indications apart from rCDI include chronic inflammatory bowel disease and the potential to benefit other functional GI disorders. Despite a widespread belief that FMT is safe, several serious adverse events (SAEs) associated with FMT have been reported. The current research aims to investigate the safety of FMT via a comprehensive analysis of the preceding studies to guide the development of carrying out FMT in a safe manner.

The presumed treatment mechanism of FMT is the establishment of a new gut microbiota to restore normal gut function, thereby eliminating CDI [28]. Studies have suggested that FMT can deliver gut bacteriophages and viruses that prompt changes in the metabolism and receding inflammation in the recipient. Donor feces have been assessed for both infectious and non-infectious risks in several clinical studies. As a feces derivative, there is the potential for donor feces to transmit numerous pathogens, including prions. Concerns have been raised about FMT recipient developing lasting alterations to the resistome. Early research suggested that the long-term effect on the gut microbiome from a single FMT could be long-lasting. Insufficient donor selection was identified as a significant safety concern in a review of eight clinical trials. Rare adverse events in studies can be traced back to inappropriate screening and testing. Interim analysis suggested that the failure of FMT safety is connected to inadequate donor screening and transmission of diseases.

15. Role of Gut Microbiota in Specific Diseases

Many posterior studies have presented the relevance of the microbiome in ecological, evolutionary, and anthropological aspects, thereby emphasizing the important implications on medicine. It has been generally speculated that the co-evolution of microbe-host towards mutualism has been driven by both complex and computable adaptive mechanisms. Disruptions, however, may lead to an evolutionary conflict resulting in the disruption of immune function, potentially enhancing susceptibility to infection. The occurrence of such events, either even a partially beneficial microorganism, antibiotic administration, or coinfection with parasitic organisms, may inadvertently have severe health implications beyond that immediately apparent. It is further postulated that such conflicts may be integral in the manifestation of allergies. Subsequent laboratory-based macaque studies support this contention [1]. Recent investigations studying the human microbiome utilizing next generation sequencing and mass spectroscopy have since been undertaken, and such research is generally at its preliminary stage. These endeavors have indicated the previously unforeseen diversity, complexity, and temporal instability in community composition. Hence, there are popular observations that the immediate environment, age, diet, health status, and epigenetic factors exert a substantial impact on the perturbation of their respective microbial communities. Microbial community spleenware and its diverse interactions allow exploitation of the metabolic capacity from a multitude of microorganisms beyond the genomic expression capacity of the human genome. Fermentation activities of this community have been implicated in the synthesis of intermediary metabolites postulated to play important roles in host biology. Experimental modeling based on a dual ecological and systems biology approach allows the formulation of in silico hypotheses regarding previously unidentified metabolic consequences of microbiome perturbation. These hypotheses hence provide a roadmap for subsequent in vitro experimentation based on a synthetic microbial ecosystem. On the other hand, the microbiome and the mammalian system have evolved together in a symbiosis that may be driven from the host side by mechanosensing and patterning signals and by selective processes exerted by the microorganisms. In summary, the interest of clinical and health-related research relies on the microbiomes' putative roles in the modulation of normal physiology, wellness, and disease state.

16. Future Directions in Gut Microbiota Research

Large-scale human microbiome projects have enabled a thorough analysis of the human microbiome across different body sites in individuals of different geographical origins, ethnicities, ages, and states of health or disease. In past years, this effort has generated a considerable amount of multi-omics data and findings associated with the human microbiome and its individual members. These findings, which have mostly been generated by taxonomic characterization and genome-scale sequencing of the microbiota, have deepened the current understanding of the human microbiome and its implications on health and disease [29]. In this regard, the human gut microbiome has emerged as a substantive research frontier with research progressing toward a more mechanistic understanding of the role of the microbial ecosystem in human health.

Therefore, the latest results stemming from human microbiome research can now be passed on to the public through different means. This information can be relevant for understanding the dynamics of what happens during microbiome-associated health or disease, which can also be significant for the improvement of existing knowledge of interactions between intestinal bacteria and the host [30]. There is also a growing interest among the general public on personalized preventive medicine/individualized health care, and the microbiome may play a critical role. Inspired by Fellows of the Centre for Bioinformatics & Computational Biology at the University of Maryland, potential research areas for future exploration can be prospected.

17. Conclusion

Understanding the Role of the Human Gut in Wellness and Disease

There is a growing understanding of the importance of the human internal microbiome in terms of normal body functioning and its association with specific diseases. Investigators found a clear link between changes in gut microbiota and 'metabolic disturbances of obesity' in both animal and large human studies. Together this research helped to characterise the human gut microbiome and the many symbiotic relationships formed with the host and their role in disease states. While the gut microbiome in animals was able to be altered in order to mimic metabolic features associated with obesity, the ability to detect/confirm such evidence in the human microbiome is still at its infancy. Nevertheless, such knowledge implies an intrinsic relationship between metabolic functions of the gut microbiota and fat storage in the midst of chronic nutrient overload, and may lend insight towards developing strategies to utilise the gut microbiome in diagnostic and therapeutic means.

For more than a century, scientists have appreciated the fact that millions of bacteria, viruses, and fungi inhabit the human body, outnumbering the host cells by tenfold. Fostered by the advent of large-scale metagenomics projects in the previous decade, a new horizon in the study of human internal microbiome has rapidly emerged . The composition of the human microbiome and its corresponding metagenome are known to be highly complex, unique, and diverse depending on niche location. There are an estimated 1,000 bacterial, archaeal, viral, and eukaryotic species residing in the human gut, primarily composed of phyla Bacteroidetes and Firmicutes. Due to their ability to convert dietary components and endogenously secreted host molecules into short-chain fatty acids, these two phyla are considered beneficial to the wellbeing of the host. On the contrary, other phyla, such as Proteobacteria and Actinobacteria, exist in smaller but similar proportions and are prevalent in gut microbiota of diseased individuals. It is also now widely acknowledged that the gut microbiota substantially affects host physiology.

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