

Significance of gut microbiota in human health and illness

Mushkan¹, Sounak Chakraborty¹, Rupesh Dutta Banik^{1*}

¹Department of Microbiology, School of Life Sciences, Swami Vivekananda University, Barrackpore, West Bengal- 700121

*Corresponding author at: Department of Microbiology, School of Life Sciences, Swami Vivekananda University, Barrackpore, West Bengal- 700121. *Corresponding Email: rupeshduttabanik99@gmail.com*

ABSTRACT

The immune system and commensal microbiota are constantly interacting, with the former teaching the latter how to react to antigens. The human gut is home to a diverse range of microorganisms that are now understood to be important for the human host by controlling immunological homeostasis and metabolic processes. Manipulation of the intestinal microbiota has been shown to change host immune cell homeostasis in mouse studies. Furthermore, metagenomic-sequencing analysis has shown that patients with obesity, asthma, and inflammatory bowel disease have different gut flora. A weakened immune response and decreased tolerance to commensal microbes are the outcomes of disruptions in the composition of the microbiota. A number of tactics, including probiotic medication, nutrition, and antibiotic use, have been used to prevent or treat chronic inflammatory disorders because of the changed microbiota composition linked to certain inflammatory diseases. Presenting and discussing current data demonstrating that the gut microbiota regulates immune system activity is the aim of this study.

Keywords: *Microbiota, homeostasis, metagenomic sequencing, gut flora, chronic disorders.*

INTRODUCTION

In an environmental niche, the collective genomes of microorganisms are referred to as the “microbiome,” while the microorganisms themselves are known as the “microbiota” (Sarkar et al. 2021; Pallister et al. 2016). Beginning in early childhood, the signature core microbiome is established and linked to early life events and maternal pregnancy-related factors, including delivery type, formula feeding, gestational age (GA), adverse childhood experiences, antibiotic exposure, and ecological factors (Sarkar et al. 2021). The human microbiome is essential to human health because, depending on its precise makeup, it can have trophic, protective, and metabolic roles (Laing et al. 2018). The human gut’s microbiota ecosystem depends heavily on gut bacteria (Zhang et al. 2015). The intestinal microbiota of humans is vast, varied, and ever-changing, containing around 100 trillion microorganisms, including at least 1000 distinct species (Li et al. 2022). The muscularis mucosae, lamina propria, and epithelial cells make up the human gut mucosa. It is colonized by 10^{14} microbes, which are ten times more numerous than human cells (Zhang et al. 2015; Tlaskalová-Hogenová et al. 2011; Singh et al. 2017). The large intestine contains by far the greatest number of microorganisms found in the human body (Pallister et al. 2016). Human health depends on the large and varied microbial community that lives in the intestines and has coevolved with our species (Kinross et al. 2011). *Firmicutes*, *Bacteroidetes*, *Actinobacteria*, and *Proteobacteria* are the four bacterial phyla that dominate the gut microbiome of the majority of mammals (Ferreira et al. 2014; Cenit et al. 2014; Zhang et al. 2015; Kinross et al. 2011; Tlaskalová-Hogenová et al. 2011). An imbalance in the normal gut microbiota has been connected to larger systemic disease manifestations like obesity, type 2 diabetes, cardiovascular disease, allergic reactions, and neurodegenerative diseases, as well as digestive issues such as inflammatory bowel illness and irritable bowel syndrome (IBS) (Aron-Wisniewsky et al. 2016; Sarkar et al. 2021; Laing et al. 2022; Jovel et al. 2018). The majority of the gut microbiota is found in the gastrointestinal tract, and it is essential to gastrointestinal disorders (Chen et al. 2023). There is mounting evidence that the microbiota determines the age

at which symptoms appear and that they are involved in chronic illnesses, such as IBD. Additionally, the microbiota may be a key target for treatment. While the selective use of probiotics, prebiotic foods, and/or supplements that less invasively change the gut flora may be more pleasant, fecal transplants have in fact been proposed for IBD and other disorders (Laing et al. 2022).

Early gut microbiome and chronic illness associations

There is evidence that the gut microbiome affects numerous physiological, metabolic, and immunological processes over the last ten years. The effect that the intestinal microbiome has in early life is therefore the subject of extensive research (Sarkar et al. 2021). Human gut microbiota has been linked to an apparently growing variety of illnesses, disorders, and functional abnormalities. Numerous factors, including age, nutrition, and medication, are known to contribute to enhanced discrete and long-lasting inflammation, in addition to genetic susceptibility, trauma, and numerous stress factors (both physical and emotional) (Bengmark 2013). The subsequent segment concentrates on providing an overview of the correlations that have attracted the most attention: the potential association between the intestinal microbiota and (1) chronic gastrointestinal disorders like IBS and IBD, and (2) systemic metabolic disorders like type 2 diabetes and obesity (Jovel et al. 2018).

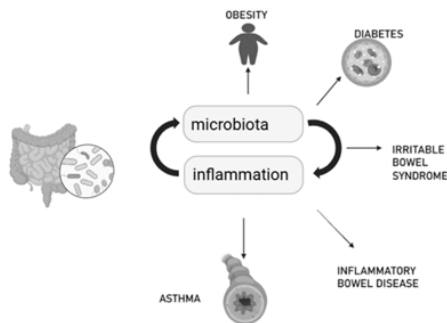


Fig.1: Role of microbiota in various chronic illness.

Inflammatory bowel disease (IBD)

The developed nations of Scandinavia, the United States, and Europe have the highest rates of inflammatory bowel disease (IBD) (Zhang et al. 2015). IBD disorders, which include Crohn's disease and ulcerative colitis, are hyperimmune, multifactorial conditions. With significant hereditary roots, these conditions are linked to inflammation and changes in the gut microbiota and metabolome (Ferreira et al. 2014; Sarkar et al. 2021; Durack et al. 2019). Anywhere along the GIT's length, CD is typified by an inflammatory pattern resembling cobblestones, with healthy tissue interspersed between the afflicted areas. Moreover, ulcerations that may cover the entire intestinal wall and cause fissures that could pierce the wall and affect other organs like the kidney or uterus are characteristic of it. Contiguous inflammation affecting mainly the intestinal wall's outer layers is the usual manifestation of UC. The rectum is where it usually starts and is mostly found in the colon (Jovel et al. 2018). Even in healthy individuals, certain microbiota composition is at risk due to genes known to be linked to IBD. Patients have been seen to have reduced microbial diversity and *Roseburia* abundance. Childhood and adolescence may be the initial stages of these illnesses, which can manifest as chronic, relapsing conditions that last a lifetime (Sarkar et al. 2021).

Irritable bowel syndrome (IBS)

The main symptoms of IBS include discomfort, pain, and changes in bowel movements. Despite having a complex etiology, new research on the pathophysiology of IBS has shown that changes in the normal gut microbiota may contribute to the syndrome's low-grade intestinal inflammation (Vijay et al. 2022; Jovel et al. 2018). It is estimated that 10% to 20% of adults and adolescents worldwide suffer from IBS. IBS is believed to have a complex etiology, while the precise cause is unknown. It is believed to develop due to a combination of genetic factors, GIT motor dysfunction, visceral hypersensitivity, infection, inflammation, immunity, and psychopathological causes (Jovel et al. 2018).

Table 1: Etiological classification of symptoms of IBS (Jovel et al. 2018).

IBS Subtype	Characteristics
IBS with constipation (IBS-C)	• More prevalent in women • Up to one-third of cases • Hard stools >25% of the time and loose stools <25% of the time
IBS with diarrhea (IBS-D)	• Up to one-third of cases • more common in men • loose stools >25% of the time and hard stools <25% of the time
Mixed IBS (IBS-M)	• Over 25% of the time, both hard and soft stools • Approximately one-third to half of cases
Unsubtyped IBS	• Stool consistency is not atypical enough to satisfy the requirements.

Obesity

The prevalence of obesity has skyrocketed, surpassing 20% in the majority of western nations. It is distinguished by an excessive or aberrant buildup of fat that has a detrimental impact on health. Lowered life expectancy and/or increased health issues, including heart disease, type 2 diabetes, obstructive sleep apnea, some cancers, and osteoarthritis, are caused by such disorders (Ferreira et al. 2014). The gut microbiota’s composition is believed to play a role in the development of obesity, and the extensive use of antibiotics in the treatment of infectious disorders as well as industrial exposure to antibiotics can contribute to the development of obesity (Sarkar et al. 2021). The development of obesity is a complicated process that mostly combines genetic predisposition, inactivity, and excessive food and energy intake (Ferreira et al. 2014). Studies in humans and animals have linked obesity to various alterations in the composition of the gut microbiota as well as a decrease in bacterial diversity.

It has been noted that obese people have higher amounts of *Firmicutes* and lower levels of *Bacteroidetes* than lean people (Cenit et al. 2014; Sarkar et al. 2021; Zhang et al. 2015).

Diabetes

Obesity from a high-fat diet is linked to inflammation, which ultimately results in the development of insulin resistance and type-2 diabetes (T2D). The metabolic disorder known as diabetes has been a major global concern and has been found to be closely linked to gut flora. Diabetes can be divided into two types: type-1 diabetes (T1D) and type 2 diabetes. Diabetes is a result of alterations in gut flora (Murphy et al. 2015; Zhang et al. 2015). T-cells destroy the pancreatic beta cells that produce insulin, causing type 1 diabetes (T1D), an autoimmune condition (Cenit et al. 2014; Sarkar et al. 2021). Type 2 diabetes is a complicated condition that is impacted by both environmental and genetic factors. It has grown to be a significant global public health issue (Jovel et al. 2018). Compared to healthy controls, those with type 2 diabetes have a different composition of gut bacteria. But it's unclear if these changes are a cause or a consequence, so more research is needed. Of the frequently reported results, T2D was negatively correlated with the genera *Bifidobacterium*, *Bacteroides*, *Faecalibacterium*, *Akkermansia*, and *Roseburia*, whereas T2D was positively correlated with the genera *Ruminococcus*, *Fusobacterium*, and *Blautia* (Vijay et al. 2022). The two helpful genera most commonly mentioned in T2D research are *Bacteroides* and *Bifidobacterium* (Gurung et al. 2020). The century's greatest epidemic is thought to be diabetes. Chronic hyperglycemia brought on by improper insulin secretion, function, or a combination of the two is a hallmark of the metabolic illness group known as diabetes. As an anabolic hormone, insulin plays a crucial role in the metabolism of proteins, fats, and carbohydrates (Sarkar et al. 2021).

Atopic asthma

Chronic asthma is characterized by increased mucus production, eosinophilia, and excessive contraction of the smooth muscle of the airways (known as airway hyper

responsiveness, or AHR). A Th-2-type inflammatory condition is asthma (Ferreira et al. 2014; Bora et al. 2023). There are other types of asthma, including nocturnal occupational asthma, non-allergic asthma, and pregnant asthma (Bora et al. 2023). In recent decades, the prevalence of asthma has rapidly increased in industrialized nations, especially among pediatric populations. This growth is believed to be attributable to changing environmental exposures associated with Western lifestyles rather than only genetic risk factors (Durack et al. 2019). The immunology of the airways is significantly impacted by the gut microbiome. Since genetic polymorphisms and environmental variables are important in the diagnosis and treatment of asthma, it is crucial to take the host microbiota's composition into account as well (Ferreira et al. 2014).

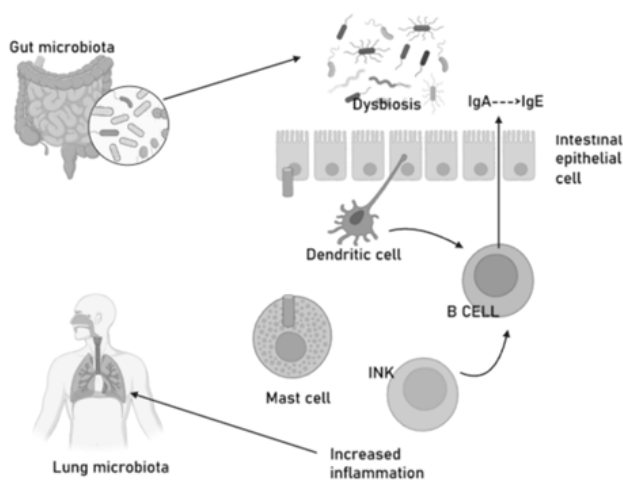


Fig.2: Role of gut microbiome in atopic asthma.

Implications of gut microbiota modification for therapy

The gut microbiota may have a therapeutic role in human health, which has given rise to therapeutic strategies like

bioecological management and bacteriotherapy. According to these beliefs, prebiotics, probiotics, and synbiotics, as well as the host's pre-morbid gut microbiota, may improve human health by modifying intestinal floral populations (Durack et al. 2019; Jovel et al. 2018). Protozoa, viruses, fungi, bacteria, and archaea make up the gut microbiota, which interacts with the host to affect its physiology and general health. When there are erratic changes in the gut ecology, GM modulation is detrimental. Probiotics led to a high-fat diet, which altered the GM structure. GM modification alleviates a number of health issues (Bora et al. 2023). A clear possible intervention that could affect the meta-organismal pathway is altering dietary nutrient intake (Tang et al. 2014).

CONCLUSION

Evolution of the human gut microbiota during the course of a person's life and seem to be crucial for both health and illness. The specific role of the gut microbiota in these diseases is unknown, but a dysbiotic state of the gut microbiota is increasingly understood as an environmental factor that interacts with a host's metabolism and plays a role in pathological conditions, including gut-related IBS and IBD as well as systemic conditions like obesity, diabetes, and atopy. Chronic inflammatory disease has been the subject of extensive investigation due of the disease's renewal and the uncertainty surrounding its beginning timing and mechanism. The results demonstrate that the development and resolution of persistent inflammation are inextricably linked to the equilibrium of intestinal microecology. Dietary and pharmaceutical intake, a sound genetic metabolism, and a healthy lifestyle are the main factors that guarantee this equilibrium.

FUTURE PROSPECTS

Over the past decade, there has been a notable surge in the scientific and clinical significance of the role of the complete microbiome in health and illness. The human immune system is now clearly impacted by alterations in gut microbiota, which can influence the onset of inflammatory and autoimmune disorders both inside and outside the gut. Despite the amazing

complexity of the gut's microbial communities, new options to define the human gut microbiota without performing cultures have been made possible by developments in next-generation sequencing and enhanced bioinformatic techniques. In order to improve cardiometabolic and inflammatory health outcomes, it is very likely that dietary therapies particularly aimed at raising specific bacterial metabolites will be developed within the next five years. The accumulation of slowly evolving, chronic pathophysiological alterations that have their roots in early life is the cause of many of the diseases currently thought to be connected to the early gut microbiota. Future tactics include converting this growing corpus of data into treatments that disrupt and modify the early gut microbiota.

Conflict of interest

There is no conflict of interest related to the study.

Author contributions

Acquisition and interpretation of data is done by Mushkan and Sounak Chakraborty. Conception, design and revising of the article are done by Rupesh Dutta Banik.

Acknowledgement

I would like to express my special thanks of gratitude to the higher dignitaries of Swami Vivekananda University for allowing me to carry out the study.

REFERENCES

- Aron-Wisnewsky, J., & Clément, K. (2016). The gut microbiome, diet, and links to cardiometabolic and chronic disorders. *Nature Reviews Nephrology*, 12(3), 169-181, DOI: 10.1038/nrneph.2015.191.
- Bengmark, S. (2013). Gut microbiota, immune development and function. *Pharmacological research*, 69(1), 87-113, DOI: 10.1016/j.phrs.2012.09.002.
- Bora, G., Gunna, A., Kumar, M. M., Morya, S., Awuchi, C. G., & Mena, F. (2023). The Gut microbiota and chronic diseases: Role of probiotics: Gut Microbiota. *Journal of Applied and Natural*

Science, 15(2), 692-703, DOI: 10.31018/jans.v15i2.4540.

Cénit, M. C., Matzaraki, V., Tigchelaar, E. F., & Zhernakova, A. (2014). Rapidly expanding knowledge on the role of the gut microbiome in health and disease. *Biochimica et Biophysica Acta (BBA)-Molecular Basis of Disease*, 1842(10), 1981-1992, DOI: 10.1016/j.bbadis.2014.05.023.

Chen, J., Xiao, Y., Li, D., Zhang, S., Wu, Y., Zhang, Q., & Bai, W. (2023). New insights into the mechanisms of high-fat diet mediated gut microbiota in chronic diseases. *iMeta*, 2(1), e69, DOI: 10.1002/imt2.69.

Durack, J., & Lynch, S. V. (2019). The gut microbiome: Relationships with disease and opportunities for therapy. *Journal of experimental medicine*, 216(1), 20-40, DOI: 10.1084/jem.2018044.

Ferreira, C. M., Vieira, A. T., Vinolo, M. A. R., Oliveira, F. A., Curi, R., & Martins, F. D. S. (2014). The central role of the gut microbiota in chronic inflammatory diseases. *Journal of immunology research*, 689492, DOI: 10.1155/2014/689492.

Gurung, M., Li, Z., You, H., Rodrigues, R., Jump, D. B., Morgun, A., & Shulzhenko, N. (2020). Role of gut microbiota in type 2 diabetes pathophysiology. *EBioMedicine*, 51, DOI: 10.1016/j.ebiom.2019.11.051.

Jovel, J., Dieleman, L. A., Kao, D., Mason, A. L., & Wine, E. (2018). The human gut microbiome in health and disease. *Metagenomics*, 197-213,

Kinross, J. M., Darzi, A. W., & Nicholson, J. K. (2011). Gut microbiome-host interactions in health and disease. *Genome medicine*, 3, 1-12,

Laing, B., Barnett, M. P., Marlow, G., Nasef, N. A., & Ferguson, L. R. (2018). An update on the role of gut microbiota in chronic inflammatory diseases, and potential therapeutic targets. *Expert Review of Gastroenterology & Hepatology*, 12(10), 969-983, DOI: 10.1080/17474124.2018.1505497.

Li, J. S., Su, S. L., Xu, Z., Zhao, L. H., Fan, R. Y., Guo, J. M., ... & Duan, J. A. (2022). Potential roles of gut microbiota and microbial metabolites in chronic inflammatory pain and the mechanisms of therapy drugs. *Therapeutic Advances in Chronic Disease*, 13, DOI: 10.1177/20406223221091177.

Murphy, E. A., Velazquez, K. T., & Herbert, K. M. (2015). Influence of high-fat diet on gut microbiota: a driving

force for chronic disease risk. *Current Opinion in Clinical Nutrition & Metabolic Care*, 18(5), 515-520, DOI: 10.1097/MCO.0000000000000209.

Pallister, T., & Spector, T. D. (2016). Food: a new form of personalised (gut microbiome) medicine for chronic diseases? *Journal of the Royal Society of Medicine*, 109(9), 331-336, DOI: 10.1177/0141076816658786.

Sarkar, A., Yoo, J. Y., Valeria Ozorio Dutra, S., Morgan, K. H., & Groer, M. (2021). The association between early-life gut microbiota and long-term health and diseases. *Journal of clinical medicine*, 10(3), 459, DOI: 10.3390/jcm10030459.

Singh, R. K., Chang, H. W., Yan, D. I., Lee, K. M., Ucmak, D., Wong, K., ... & Liao, W. (2017). Influence of diet on the gut microbiome and implications for human health. *Journal of translational medicine*, 15, 1-17, DOI: 10.1186/s12967-017-1175-y.

Tang, W. W., & Hazen, S. L. (2014). The contributory role of gut microbiota in cardiovascular disease. *The Journal of clinical investigation*, 124(10), 4204-4211, DOI: 10.1172/JCI72331.

Tlaskalová-Hogenová, H., Štěpánková, R., Kozáková, H., Hudcovic, T., Vannucci, L., Tučková, L., ... & Funda, D. P. (2011). The role of gut microbiota (commensal bacteria) and the mucosal barrier in the pathogenesis of inflammatory and autoimmune diseases and cancer: contribution of germ-free and gnotobiotic animal models of human diseases. *Cellular & molecular immunology*, 8(2), 110-120, DOI: 10.1038/cmi.2010.67.

Vijay, A., & Valdes, A. M. (2022). Role of the gut microbiome in chronic diseases: a narrative. *European journal of clinical nutrition*, 76, 489-501,

Zhang, Y. J., Li, S., Gan, R. Y., Zhou, T., Xu, D. P., & Li, H. B. (2015). Impacts of gut bacteria on human health and diseases. *International journal of molecular sciences*, 16(4), 7493-7519, DOI: 10.3390/ijms16047493.