Gut Microbiome, a Link between Nutrition, Physiology, and Pathology: Insights into Current Status and Future Directions

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Abstract

The gut and placental microbiome have emerged as key determinants of human health and well-being, with their beneficial effects extending well beyond the confines of the digestive and reproductive systems. Recent advances in microbial research have revealed that these microbial communities play crucial roles in nutrient absorption, immune modulation, and even neurobehavioral processes. By regulating the host-microbe interaction and maintaining a balance between commensal and pathogenic bacteria, the gut microbiome is vital for maintaining optimal health and preventing a host of chronic diseases. Dietary fiber plays a critical role in promoting a diverse and healthy gut microbiome, which confers many health benefits to the host. This review article delves into the different functions that gut microbiota can potentially perform in shaping our health status and the implications of gut microbiome disturbances on human health in the form of various gastrointestinal as well as extra-intestinal diseases. Furthermore, we shed light on current scientific investigations that have widened our grasp of the human microbiome, specifically cutting-edge molecular sequencing technology, and analytical approaches. A more nuanced comprehension of this intricate concept harbors diagnostic and therapeutic implications for various pathogenic pathways linked to inflammatory and neoplastic diseases.

Keywords: Gut microbiota • Short-chain fatty acids • Microbiota-accessible carbohydrates • Obesity • Diabetes • Asthma • Autism spectrum disorder • Alzheimer's disease • Metagenomics analysis

Introduction

Microbiotas are the symbiotic organisms of thousands of species that are abundantly present inside and outside the human body, coexisting harmoniously while performing multiple functions that are crucial for optimal physiological processes and well-being. The gut microbiota has been shown to influence various aspects of human physiology, including metabolism, immunity, and brain function. These microorganisms include bacteria, fungi, and viruses, and interestingly, their population in the human body surpasses that of human cells [1]. The human microbiome comprises approximately 10 trillion-100 trillion symbiotic microbial cells present in each individual, making the number of microbial cells in our body more than that of human cells. The human gut alone accommodates up to 1,000 species of microbiota that perform diverse functions [2]. Microbiomics is an expanding discipline that involves investigating these organisms, their roles, and their effects on the human body.

Beginning in the 1680s, when Antonie van Leeuwenhoek compared his oral and fecal flora, research on the diversity of the human microbiome began. He observed the considerable variations in microorganisms between these two habitats as well as between samples from people in healthy and diseased stages in both of these locations [3,4]. Research into the remarkable differences between microorganisms in various anatomical locations, and the differences between their roles in health and disease, dates back to the earliest days of microbiology. However, recent cutting-edge breakthroughs in technology have enabled us to utilize powerful molecular tools to investigate the underlying reasons behind these distinctions and even manipulate the transformations between states. It is not the observation of these evident contrasts that is groundbreaking today, but rather the ability to elucidate the mechanisms that give rise to them. The mutual evolution of vertebrates and their associated microbial communities, spanning over hundreds of millions of years, has resulted in a distinct microbial consortium that thrives in the gut's stable, nutrient-rich, and warm surroundings. While archaea, eukaryotes, and viruses are also present in the gut, albeit in smaller quantities and should not be overlooked, bacteria comprise the bulk of the biomass and diversity within the human gut and in all other ecosystems that are interconnected with human beings [5-7].

While there are some microorganisms that are pathogenic, it is worth noting that both symbiotic and pathogenic microbiota coexist. There is a complex interplay between symbiotic and pathogenic microorganisms within the human body. The vast majority of the microbiome comprises of beneficial and symbiotic microorganisms that provide advantages to both the host and the microbiota. However, symbiosis can occur due to certain infectious diseases, poor diets, or prolonged usage of antibiotics or other antibiotic-like drugs. This can render an individual more susceptible to a range of diseases, varying in severity from mild to severe [8-11].

One of the most widely scrutinized topics pertaining to the human microbiome is the gut. This manuscript furnishes comprehensive details about the gut microbiome, its diversity, and its influence on human well-being and pathological conditions. It also explores the placental microbiome, its potential role in neonatal gut colonization, the development of the microbiota from infancy through early childhood, and the impact of various factors, such as birth mode and diet.

Literature Review

Fiber, fatty acids, and the gut microbiota: How they shape our health

The gut microbiome is a complex and diverse community of microorganisms that plays a critical role in the regulation of digestion, immunity, and other important bodily processes throughout life. It is an amalgamation of diverse and fluctuating microorganisms which vary according to numerous factors including age, sex, race, ethnicity, gender, and lifestyle choices such as the use of alcohol, smoking, and physical activity, as well as geographical location and medications [12].

Research has shown that an imbalance in the gut microbiota can have negative effects on health, contributing to the development of various diseases, including obesity, diabetes, and inflammatory bowel disease. On the other hand, a healthy gut microbiome can help prevent these diseases and promote overall well-being. Studies have also highlighted the impact of various factors on the gut microbiome, including diet, antibiotic use, age,

and environmental factors such as sanitation. For example, a study published in Nature Microbiology found that the gut microbiota of individuals in developed countries is less diverse than those in less developed areas due to factors such as increased hygiene practices and a more processed diet [13-15].

Hippocrates studied the gastrointestinal properties of coarse wheat versus refined wheat in 430 BC, while J.H. Kellogg wrote numerous articles on the benefits of bran in the 1920s, asserting that it boosts stool weight, facilitates laxation, and prevents illnesses [16]. The 1930s saw extensive research on dietary fiber, however, afterward it was neglected until the 1970s. Diet significantly influences the types of bacteria that exist in the colon, in addition to environmental factors, medication use, and genetics from the family[17,18].

A higher intake of dietary fiber plays a crucial role in the prevention of cardiovascular diseases and in maintaining gut health. Regularly consuming the recommended amount of fiber has the potential to attenuate glucose absorption rate, prevent weight gain, and increase the intake of beneficial nutrients and antioxidants in the diet, all of which may help prevent diabetes. Dietary fibers exhibit a diverse range of physicochemical properties and corresponding physiological effects [19,20]. Martinez et al performed a study that used 16S rRNA gene sequencing to analyze the gut microbiota of healthy individuals after a whole grain intervention and found that the whole grain diet increased the abundance of specific bacterial taxa, which were associated with improved immune function and lower inflammation[21]. Another study analyzed data from 185 observational studies and 58 clinical trials to evaluate the effects of different types of carbohydrates, including fiber, on various health outcomes. The authors found that higher intakes of dietary fiber were associated with lower risks of cardiovascular disease, type 2 diabetes, and colorectal cancer [22]. The effects of dietary fiber on hunger, satiety, energy intake, nutrient absorption and body composition in healthy individuals are well documented [23,24]. Dietary fiber can also promote weight loss or prevent weight gain. Other less well-known health benefits of dietary fiber include its effects on immune function, bone health, and cognitive function [25].

Role of Short-Chain Fatty Acids (SCFA)

The microbiota in the colon digests the fiber, producing short-chain fatty acids that contribute to shaping the gut environment, influencing the physiology of the colon, and eventually serving as an energy source for host cells. By playing an important role in different host-signaling mechanisms, these fatty acids have enormous potential for promoting a healthy body [26,27]. Microbial degradation of dietary fiber in the gut is a complex process, including the role of different microbial populations in breaking down and fermenting different types of fiber. Since dietary fiber can only be broken down and fermented by enzymes from microbiota living in the colon that eventually release SCFAs, the pH of the colon becomes more acidic, creating an environment favorable for a specific type of microbiota that can survive in the acidic conditions[28]. While some harmful bacteria cannot survive in this acidic pH, there are numerous benefits of SCFA, including stimulating immune cell activity and maintaining normal blood levels of glucose and cholesterol [29]. Numerous studies have discussed the potential for dietary interventions targeting SCFA production to improve metabolic health [30-32].

The crucial role of gut microbiome in maintaining optimal health from the beginning

The gut microbiome holds sway over the human physique from the moment of birth and persistently influences vital bodily functions such as the digestive, immune, and central nervous systems [33-35]. The placenta was once thought to be sterile, but recent studies have shown that it harbors a diverse microbiome that can impact fetal development. Despite its manifold metabolic and immunological regulating functions, the placental microbiome's compositional and functional diversity remains relatively underexplored. Impactful research has nonetheless evinced a correlation between placental microbiota and antenatal infection history, maternal weight gain, and the altered placental membrane microbiome seen in preterm birth, which remains a significant cause of neonatal morbidity and mortality [36-41] .The early microbial composition of neonates is significantly influenced by both delivery method and gestational age. The mode of delivery, whether vaginal or caesarean, plays a crucial role in determining the initial contact between the fetal body and the microbiome, with the former more closely resembling the maternal flora. Interestingly, infants delivered by cesarean section exhibit a gut flora composition that is less similar to their mothers compared to those delivered vaginally [42-44].

From the moment of birth, a newborn is surrounded by microorganisms, and as the child grows, the gut microbiota begins to colonize [45-47]. The adult gut microbiome, which is influenced by important factors such as an increase in the abundance of Bacteroidetes, elevated fecal SCFA levels, enrichment of genes related to carbohydrate utilization, vitamin biosynthesis, and xenobiotic degradation, is reliant on oral feeding. The composition of the microbiota is significantly influenced by prolonged nursing, which is crucial for the structure and function development of the microbiome [48-50] . Breast milk is rich in chemicals that play a vital role in promoting the growth of *Bifidobacteria* and *Bacteroides* [51,52]. Despite being able to digest lactose, the infant's small intestine lacks the glycoside hydrolases and intestinal membrane transporters needed to break down the human milk oligosaccharides. As a result, milk glycans can increase the number of bacteria in the gut microbiota that break down complex carbohydrates [53]. The introduction of solid food and the cessation of breastfeeding results in a shift in their composition to an adult-like microbiota [54-56]. Variations in the microbial community during the first months are driven by factors such as sanitary conditions or antibiotic use. [57-59] The mechanisms linking these and other important factors to the construction of the microbiota are still being investigated.

Factors that impact gut microbiota and disease

The gut microbiome is impacted by a variety of factors, including stomach pH, bile acids, digestive enzymes, and antimicrobial proteins in the duodenum, among others. Other major variables can also affect microbial colonization further downstream, such as chemical parameters like pH, oxygen concentrations, mucus, and antibodies, as well as anatomical abnormalities related to gut receptors, immune cells, and nerve cells. These factors can ultimately influence gut peristalsis and transit times, playing an essential role in the alteration of the microbiome and host relationship [60-62].For instance, Sonnenburg, E.D. et al describe in their article how a diet deficient in Microbiota-Accessible Carbohydrates (MACs) can affect the composition and function of the gut microbiota and ultimately alter the host-microbe relationship [63]. Consequently, the gut microbiome has emerged as a significant factor in various metabolic and immune diseases.

Gastrointestinal diseases and diseases of the hepatobiliary system, including intestinal bowel diseases, celiac disease, irritable bowel syndrome, colorectal cancer, chronic liver diseases, and pancreatic disorders, have been linked to the gut microbiota [64,65]. Various extra-intestinal disorders, such as obesity and obesity-related disorders like type 2 diabetes and non-alcoholic fatty liver disease, have also been linked to the gut microbiome, mainly due to its effects on glucose regulation and correlation with insulin resistance [66-70]. Ley R. E. discussed in their article the role of microbiota in energy metabolism, particularly in the context of obesity. The author also describes the potential mechanisms by which gut microbiota may contribute to the development of obesity, including increased energy harvest and storage, altered gut hormone signaling, and inflammation [71].

Extraintestinal pathology due to gut microbiota dysbiosis

Respiratory Conditions: Susceptibility for development of asthma has been noted in neonates and infants who have correlations with gut microbiome dysbiosis, including microbial depletion and fungal overgrowth. In their infancy, these neonates' fecal metabolic profile exhibited a deficiency of omega-3 fatty acids and prostaglandin precursors [72]. Numerous researchers have shared profound insights regarding the interplay between environmental pollution, gut microbiota, and allergic bronchitis/asthma [73,74]. Multiple studies have revealed that the administration of vancomycin was connected to a reduction in gut microbial diversity, altered metabolic profiles, intensified Th2 responses, and an elevated likelihood of allergic bronchitis [75]. The provision of SCFAs has been revealed to alleviate alveolar inflammation, primarily attributed to reduced T cell activity, specifically a decrease in IL-4-producing CD4+ T cells and decreased circulating IgE levels [76].

CNS diseases and Behavioral problems: The gut microbiota has been revealed to act as a mediator of biochemical signaling in the gut-brain axis, demonstrating an association with disrupted gut microbial homeostasis [77]. Disordered microbial flora have exhibited significantly elevated concentrations of SCFAs and ammonia, the metabolites of which may harbor a neurotoxic influence leading to various CNS disorders [78,79]. The microbial composition of the gut has been found to be intricately linked to Autism Spectrum Disorder (ASD) and other neurodevelopmental conditions characterized by aberrant behavior, cognitive impairment, and mental distress [80-84]. Presently, many researchers are investigating the relationship between the gut microbiota and stroke pathogenesis, Alzheimer's disease, as well as novel therapeutic opportunities for addressing these conditions with the prism of the gut microbiome [85,86].

Cardiac conditions: Recent studies have brought to light the fact that the gut microbiota is capable of influencing the entire host body. Over the past two decades, there has been a substantial amount of research dedicated to comprehending the evolution of gut microbiota and its implications for risk factors associated with cardiovascular diseases [87]. Substantive evidence has further validated the causal impact of the gut microbiota on Cardiovascular Disease (CVD). Notably, studies on gut microbiota transplantation, gut microbiota-dependent pathways, and downstream metabolites have demonstrated their ability to influence host metabolism and the onset of CVD. For instance, Trimethylamine N-Oxide (TMAO), a met organismal metabolite produced following the consumption of dietary nutrients prevalent in a Western-style diet, and more recently, Phenyl Acetyl Glutamine (PAG), a phenylalanine-derived metabolite, are examples of gut microbiota-dependent metabolites. Elevated levels of these metabolites in the bloodstream have been linked to increased CVD risk in large-scale clinical studies [88-90].

Revolutionizing microbiome research: The power of molecular analysis

The swift advancements in high-throughput molecular methods have facilitated in-depth analysis of the microbiota's genetic and functional diversity, enabling us to comprehend the species present, their relationships with each other, the expressed genes, and the ongoing metabolic activities [91,92]. With the advent of cutting-edge platforms such as Illumina, 454 Roche, Pac Bio, and Oxford Nano pores, we can now perform metagenomics, metatranscriptomics, met proteomics, and met metabolomics, allowing us to explore biological signatures related to specific environments [93-97].

Metagenomic analysis of gut microbiota involves sequencing the DNA of all the microorganisms present in a given sample and then using bioinformatics tools to identify and characterize the microbial community. This approach has revealed the tremendous diversity of the gut microbiota and has led to the discovery of numerous novel microbial species and genes. Metagenomic analysis has also been used to investigate the role of the gut microbiota in various diseases, including inflammatory bowel disease, colorectal cancer, and metabolic disorders [98-100]. The continual improvement of sequencing techniques and analytical approaches enhances our understanding of the human microbiome, including its definition and constituents. Furthermore, by gaining a better understanding of the gut microbiota and its functions, we may be able to develop new strategies for preventing and treating these diseases.

Conclusions

Studies are ongoing to explore the critical importance of the gut microbiome, the various ways in which the gut microbiome influences human health, and potential therapies to manipulate the microbiome to treat diseases. In the meantime, it is important to prioritize a healthy lifestyle to support the health of our gut microbiome and our overall well-being.

The swift progression of sequencing methods and analytical techniques is augmenting our capacity to understand the human microbiome, as well as our conception of the microbiome and its elements. Therefore, we believe that there is ground for cautious sanguinity that further innovations in sequencing technology and comprehension of the microbiome will present thrilling opportunities for utilizing the microbiota for personalized medicine.

Conflicts of Interest

The author declares that he has no financial or personal relationship which may have inappropriately influenced him in writing this article.

References

1. Bartlomiejczyk, Marcin Adam, et al. "Worldwide dyslipidemia guidelines." *Curr. Cardiovasc. Risk Rep.* 13 (2019): 1-7.
2. Aurigemma, Nicole C., et al. "Linking the gut microbiota to bone health in anorexia nervosa." *Curr. Osteoporos. Rep.* 16 (2018): 65-75.
3. Microscopes*, OLD. "DOWN.*
4. Dobell, Clifford. "The discovery of the intestinal protozoa of man.*" Proc. R. Soc. Med. 13.Sect_Hist_Med* (1920):
5. Ley*,* Ruth E., et al. "Worlds within worlds: evolution of the vertebrate gut microbiota.*" Nat. Rev. Microbiol. 6.10* (2008*):* 776-788.
6. Marchesi, Julian R. "Prokaryotic and eukaryotic diversity of the human gut.*" Adv. appl. microbiol. 72* (2010*): 43-62.*
7. Breitbart, Mya, et al. *"Viral diversity and dynamics in an infant gut." Res. microbiol.* 159.5 (2008*):* 367-373.
8. *Kamada, Nobuhiko, et al.* "Role of the gut microbiota in immunity and inflammatory disease.*" Nat. Rev. Immunol.* 13.5 (2013*):* 321-335.
9. Backhed, Fredrik, et al. "Host-bacterial mutualism in the human intestine.*" science* 307.5717 (2005): 1915-1920.
10. Cho, Ilseung, et al. "The human microbiome: at the interface of health and disease.*" Nat. Rev. Genet.* 13.4 (2012): 260-270.
11. Dethlefsen, Les, et al. "Incomplete recovery and individualized responses of the human distal gut microbiota to repeated antibiotic perturbation.*" Proceedings of the National Academy of Sciences 108.supplement_*1 (2011): 4554-4561.
12. Thursby, Elizabeth, et al. "Introduction to the human gut microbiota." *Biochem. j.* 474.11 (2017): 1823-1836.
13. Valles-Colomer, Mireia, et al. "The neuroactive potential of the human gut microbiota in quality of life and depression." *Nat. microbiol.* 4.4 (2019): 623-632.
14. Sonnenburg, Justin L., et al. "Diet–microbiota interactions as moderators of human metabolism." Nature 535.7610 (2016): 56-64.
15. Rothschild, Daphna, et al. "Environment dominates over host genetics in shaping human gut microbiota." Nature 555.7695 (2018): 210-215.
16. Slavin, Joanne L. "Dietary fiber: classification, chemical analyses, and food sources." *J. Am. Diet. Assoc.* 87.9 (1987): 1164-1171.
17. Tannock, Gerald W., et al. "Influences of dietary and environmental stress on microbial populations in the murine gastrointestinal tract." *Infect. immun.* 9.3 (1974): 591-598.
18. Gibson, Glenn R., et al. "Dietary modulation of the human colonic microbiota: updating the concept of prebiotics." *Nutr. res. rev.* 17.2 (2004): 259-275.
19. Wu, Gary D., et al. "Linking long-term dietary patterns with gut microbial enterotypes." Science 334.6052 (2011): 105-108.
20. Maslowski, Kendle M., et al. "Diet, gut microbiota and immune responses." *Nat. immunol.* 12.1 (2011): 5-9.
21. Martínez, Inés, et al. "Gut microbiome composition is linked to whole grain-induced immunological improvements." *ISME j.* 7.2 (2013): 269-280.
22. Reynolds, Andrew, et al. "Carbohydrate quality and human health: a series of systematic reviews and meta-analyses*," Lancet* 393.10170 (2019): 434-445.
23. Slavin, Joanne L. "Dietary fiber and body weight.*" Nutrition* 21.3 (2005): 411-418.

24. Anderson, James W., et al. "Health benefits of dietary fiber." *Nutr. rev.* 67.4 (2009): 188-205.
25. *Kaczmarczyk, Melissa M.*, et al. "The health benefits of dietary fiber: beyond the usual suspects of type 2 diabetes mellitus, cardiovascular disease and colon cancer." *Metabolism* 61.8 (2012): 1058-1066.
26. Simpson, Hannah L., et al. Campbell. "dietary fibre–microbiota interactions." Alimentary pharmacology & therapeutics 42.2 (2015): 158-179.
27. Dahl, Wendy J., et al. "Health benefits of fiber fermentation." *J. Am. Coll. Nutr.* 36.2 (2017): 127-136.
28. Flint, Harry J., et al. "Microbial degradation of complex carbohydrates in the gut." *Gut microbes* 3.4 (2012): 289-306.
29. Ríos-Covián, David, et al. "Intestinal short chain fatty acids and their link with diet and human health." *Front. microbiol. 7 (2016): 185*.
30. Blaak, E. E., et al. "Short chain fatty acids in human gut and metabolic health." *Benef. microbes* 11.5 (2020): 411-455.
31. Barrea, Luigi, et al. "From gut microbiota dysfunction to obesity: could short-chain fatty acids stop this dangerous course?." *Hormones 18 (2019): 245-250*.
32. Holmes, Zachary C., et al. "Short-chain fatty acid production by gut microbiota from children with obesity differs according to prebiotic choice and bacterial community composition." *MBio 11.4 (2020): e00914-20*.
33. Rinninella, Emanuele, et al. "What is the healthy gut microbiota composition? A changing ecosystem across age, environment, diet, and diseases." *Microorganisms* 7.1 (2019): 14.
34. Yatsunenko, Tanya, et al. "Human gut microbiome viewed across age and geography." *nature* 486.7402 (2012): 222-227.
35. Saxena, R., Saxena, R., Raj, A. *(2018).* Microbiomics in the molecular era: A bird's eye view into the future of personalized medicine. *Acta Sci. Microbiol.* 1(8), 34-39.
36. Galazzo, Gianluca, et al. "Development of the microbiota and associations with birth mode, diet, and atopic disorders in a longitudinal analysis of stool samples, collected from infancy through early childhood." *Gastroenterology* 158.6 (2020): 1584-1596.
37. Aagaard, Kjersti, et al. "The placenta harbors a unique microbiome." *Sci. transl. med.* 6.237 (2014): 237ra65-237ra65.
38. Yao, Yao, et al. "The role of microbiomes in pregnant women and offspring: research progress of recent years," F*ront. Pharmacol.* 11 (2020): 643.
39. Chu, Derrick M., et al. "Impact of maternal nutrition in pregnancy and lactation on offspring gut microbial composition and function." *Gut Microbes* 7.6 (2016): 459-470.
40. Gohir, Wajiha, Elyanne M. Ratcliffe, and Deborah M. Sloboda. "Of the bugs that shape us: maternal obesity, the gut microbiome, and long-term disease risk." *Pediatr. res. 77.1 (2015): 196-204*.
41. Nyangahu, D. D., and H. B. Jaspan. "Influence of maternal microbiota during pregnancy on infant immunity," *Clin. Exp. Immunol.* 198.1 (2019): 47-56.
42. Mitchell, Caroline M., et al. *"Delivery mode affects stability of early infant gut microbiota." Cell Rep. Med.* 1.9 (2020): 100156.
43. Rutayisire, Erigene, et al. "The mode of delivery affects the diversity and colonization pattern of the gut microbiota during the first year of infants' life: a systematic review." *BMC gastroenterol.* 16.1 (2016): *1-12*.
44. Wang, Mei, et al. "Mode of delivery and early nutrition modulate microbial colonization and fermentation products in neonatal piglets." *J. nutr.* 143.6 (2013): 795-803.
45. Koenig, Jeremy E., et al. "Succession of microbial consortia in the developing infant gut microbiome." *Proc. Natl. Acad. Sci. 108.supplement_*1 (2011): 4578-4585.
46. Ley, Ruth E., et al. "Human gut microbes associated with obesity." *nature* 444.7122 (2006): 1022-1023.
47. David, Lawrence A., et al. "Diet rapidly and reproducibly alters the human gut microbiome." *Nature 505.7484 (2014): 559-563*.
48. Boudry, Gaëlle, et al. "The relationship between breast milk components and the infant gut microbiota." *Front. nutr.* 8 (2021): 629740.
49. Corona-Cervantes, Karina, et al. "Human milk microbiota associated with early colonization of the neonatal gut in Mexican newborns." *PeerJ* 8 (2020): e9205.
50. van den Elsen, L. W. J., et al. *"Shaping the gut microbiota by breastfeeding: the gateway to allergy prevention?. Front Pediatr.* 2019; 7: 47." (2019).
51. Dominguez-Bello, Maria G., et al. "Delivery mode shapes the acquisition and structure of the initial microbiota across multiple body habitats in newborns." *Proc. Natl. Acad. Sci.* 107.26 (2010): 11971-11975.
52. Marcobal, Angela, et al. "Consumption of human milk oligosaccharides by gut-related microbes." *J. agric. food chem.* 58.9 (2010): 5334-5340.
53. German, J. Bruce, et al. "Human milk oligosaccharides: evolution, structures and bioselectivity as substrates for intestinal bacteria." *Pers. nutr. diverse needs infants child.* 62 (2008): 205-222.
54. Donovan, Sharon M., et al. "Human milk oligosaccharides influence neonatal mucosal and systemic immunity." *Ann. Nutr. Metab.* 69.*Suppl.* 2 (2016): 41-51.
55. Milani, Christian, et al. "The first microbial colonizers of the human gut: composition, activities, and health implications of the infant gut microbiota." *Microbiol. mol. biol. rev.* 81.4 (2017): e00036-17.
56. Thum, Caroline, et al. "Can nutritional modulation of maternal intestinal microbiota influence the development of the infant gastrointestinal tract?." *J. nutr.* 142.11 (2012): 1921-1928.
57. Bokulich, Nicholas A., et al. "Antibiotics, birth mode, and diet shape microbiome maturation during early life." *Sci. transl. med.* 8.343 (2016): 343ra82-343ra82.
58. Zhu, S. R., et al. "Zhonghua yu fang yi xue za zhi [Chinese journal of preventive medicine]." *Zhonghua Yu Fang Yi Xue Za Zhi* 43.9 (2009): 803-808.
59. Yassour, Moran, et al. "Natural history of the infant gut microbiome and impact of antibiotic treatment on bacterial strain diversity and stability." *Sci. transl. med.* 8.343 (2016): 343ra81-343ra81.
60. Belizário, José E., et al. "Human microbiomes and their roles in dysbiosis, common diseases, and novel therapeutic approaches." *Front. microbiol.* 6 (2015): 1050.
61. Donaldson, Gregory P., et al. "Gut biogeography of the bacterial microbiota." *Nat. Rev. Microbiol.* 14.1 (2016): 20-32.
62. O'Hara, Ann M., et al. "The gut flora as a forgotten organ." *EMBO reports* 7.7 (2006): 688-693.
63. Sonnenburg, Erica D., et al. "Starving our microbial self: the deleterious consequences of a diet deficient in microbiota-accessible carbohydrates." *Cell metab.* 20.5 (2014): 779-786.
64. Schnabl, Bernd, et al. "Interactions between the intestinal microbiome and liver diseases." *Gastroenterology* 146.6 (2014): 1513-1524.
65. Albhaisi, Somaya AM, et al. "Role of gut microbiota in liver disease." *Am. J. Physiol.-Gastrointest. Liver Physiol.* 318.1 (2020): G84-G98.
66. Bashiardes, S., et al. "Non-alcoholic fatty liver and the gut microbiota." *Mol. metab.* 5.9 (2016): 782-794.
67. Arab, Juan P., et al. "Gut microbiota in non-alcoholic fatty liver disease and alcohol-related liver disease: Current concepts and perspectives." *Hepatol. Res.* 50.4 (2020): 407-418.
68. Herbert, T. and Kaser, A. "Gut microbiome, obesity, and metabolic dysfunction." *J. clin. investig.* 121.6 (2011): 2126- 2132.
69. Cani, Patrice D., et al. "Metabolic endotoxemia initiates obesity and insulin resistance." *Diabetes* 56.7 (2007): 1761-1772.

70. Cani, Patrice D., and Nathalie M. Delzenne. "The role of the gut microbiota in energy metabolism and metabolic disease." *Curr. pharm. des.* 15.13 (2009): 1546-1558.
71. Ley, Ruth E. "Obesity and the human micr*obiome." Curr. opin. gastroenterol.* 26.1 (2010): 5-11.
72. Fujimura, Kei E., et al. "Neonatal gut microbiota associates with childhood multisensitized atopy and T cell differentiation." *Nat. med.* 22.10 (2016): 1187-1191.
73. Fujimura, K. E., and S. V. Lynch. "Microbiote dans les allergies et l'asthme et la relation émergente avec le microbiome intestinal." *Microbe hôte cell.* 17 (2015): 592-602.
74. Durack, Juliana, et al. "Airway microbiota and the implications of dysbiosis in asthma." *Curr. allergy asthma rep.* 16 (2016): 1-13.
75. Russell, Shannon L., et al. "Early life antibiotic-driven changes in microbiota enhance susceptibility to allergic asthma." *EMBO reports* 13.5 (2012): 440-447.
76. Cait, A., et al. "Microbiome-driven allergic lung inflammation is ameliorated by short-chain fatty acids." *Mucosal immunol.* 11.3 (2018): 785-795.
77. *Fung, Thomas C.,* et al. "Interactions between the microbiota, immune and nervous systems in health and disease." *Nat. neurosci.* 20.2 (2017): 145-155.
78. Caputi, Valentina, et al. "Gut microbiota as a mediator of host neuro-immune interactions: implications in neuroinflammatory disorders." *Microbes Mind* 32 (2021): 40-57.
79. Wang, Lv, et al. "Elevated fecal short chain fatty acid and ammonia concentrations in children with autism spectrum disorder." *Dig. dis. sci.* 57 (2012): 2096-2102.
80. Vuong, Helen E., et al. "Emerging roles for the gut microbiome in autism spectrum disorder." *Biol. psychiatry* 81.5 (2017): 411-423.
81. Li, Qinrui, et al. "The gut microbiota and autism spectrum disorders." *Front. cell. neurosci. (*2017): 120.
82. Li, Q., and J-M. Zhou. "The microbiota–gut–brain axis and its potential therapeutic role in autism spectrum disorder." *Neuroscience* 324 (2016): 131-139.
83. Strati, Francesco, et al. "New evidences on the altered gut microbiota in autism spectrum disorders." *Microbiome* 5 (2017): 1-11.
84. Finegold, Sydney M., et al. "Pyrosequencing study of fecal microflora of autistic and control children." *Anaerobe* 16.4 (2010): 444-453.
85. Jiang, Chunmei, et al. "The gut microbiota and Alzheimer's disease." *J. Alzheimer's Dis.* 58.1 (2017): 1-15.
86. Varesi, Angelica, et al. "The potential role of gut microbiota in Alzheimer's disease: From diagnosis to treatment." *Nutrients* 14.3 (2022): 668.
87. Witkowski, Marco, et al. "Gut microbiota and cardiovascular disease." *Circ. res.* 127.4 (2020): 553-570.
88 Koeth, Robert A., et al. "Intestinal microbiota metabolism of L-carnitine, a nutrient in red meat, promotes atherosclerosis." *Nat. med.* 19.5 (2013): 576-585.
89. Koeth, Robert A., et al "Intestinal microbiota metabolism of L-carnitine, a nutrient in red meat, promotes atherosclerosis." *Nat. med.* 19.5 (2013): 576-585.
90. Nemet, Ina, et al *"A* cardiovascular disease-linked gut microbial metabolite acts via adrenergic receptors." *Cell* 180.5 (2020): 862-877.
91. Aggarwal, Nikhil, et al. "Microbiome and human health: Current understanding, engineering, and enabling technologies." *Chem. Rev.* (2022).
92. Malla, Muneer Ahmad, et al "Exploring the human microbiome: the potential future role of next-generation sequencing in disease diagnosis and treatment." *Front. Immunol.* 9 (2019): 2868.
93. Konstantinos, M. et al. "The fast changing landscape of sequencing technologies and their impact on microbial genome assemblies and annotation." *PloS one* 7.12 (2012): e48837.
94 Saheb Kashaf, Sara, et al. "Integrating cultivation and metagenomics for a multi-kingdom view of skin microbiome diversity and functions." *Nat. microbiol.* 7.1 (2022): 169-179.
95. Arikawa, Koji, et al. *"Recovery of strain-resolved genomes from human microbiome through an integration framework of single-cell genomics and metagenomics." Microbiome* 9 (2021): 1-16.
96. Forster, Samuel C., et al. A human gut bacterial genome and culture collection for improved metagenomic analyses." *Nat. biotechnol.* 37.2 (2019): 186-192.
97. Ottman, Noora, et al. "The function of our microbiota: who is out there and what do they do?." *Front. cell. infect. microbiol. (*2012): 104.
98. Qin, Junjie, et al. "A human gut microbial gene catalogue established by metagenomic sequencing." *nature* 464.7285 (2010): 59-65.
99. Lloyd-Price, Jason, et al "Multi-omics of the gut microbial ecosystem in inflammatory bowel diseases." *Nature* 569.7758 (2019): 655-662.
100. Le Chatelier, Emmanuelle, et al. "Richness of human gut microbiome correlates with metabolic markers." *Nature* 500.7464 (2013): 541-546.

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