Pages 10-17

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Exploring the Human Microbiome: Its Role in Health, Disease, and Therapeutic Interventions

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Abstract

Advanced sequencing tools led us to study the human microbiome more deeply because they help us understand how microorganisms and genetics work together. The human microbiome field changed quickly thanks to 16S rRNA and metagenomic sequencing methods which show accurate microorganism details and help understand gene families and metabolic pathways. The study of microbial connections faces two primary challenges in determining rare organisms and ensuring standard reliable outcome measurements for microbe-wide association studies. Recorded similarities between twins help scientists understand genetic influence while research continues to measure how genes shape the microbes inside our bodies. Better medical treatment results will become possible through custom medicine development because researchers now have enough data about both microbiome composition and genetic traits. Using omics integration will become essential in microbiome genetics research to find complex connections among health patterns and host genes with microbiome composition to create better treatments. It has been concluded that The human microbiome uses its effects on mouth skin and stomach areas to shape health and wellness. Most health conditions start or become better through the presence of the microbiome which helps fight inflammatory and immune system functions. The environment and our everyday choices including diet, living habits and antibiotic use strongly shape our microbiome development. Our personal health results depend strongly on which microbes live in our bodies and these microorganisms develop naturally by our genetic make-up. Personalized microbiome treatments hold great promise to build better healthcare and show better results with patients. Further research combining various study types will help scientists better understand the association between host genes and digestive system bacteria. Through combined work between medical professionals and scientists microbiome research will expand its impact on worldwide public health while being applied in medical care.

INTRODUCTION

Bacteria and viruses along with microbial eukaryotes and archaea inhabit and work together throughout our human body. Human cells represent 5-724 billion to 30-400 trillion bacterial cells in our body (Rosner JL,2014). Research shows these microorganisms take part in different disease processes while belonging to multiple taxonomic units. Microbes within the human body can benefit each other in some cases but stay neutral or infect us. These organisms find suitable environments to colonize in the human respiratory organs, facial and vaginal lining, external skin, internal female breast and digestive system as well as other body parts (Whiteside SA, Razvi H, Dave S,2015). From birth the human body establishes a beneficial mutual connection with its natural bacteria which defends good overall health. Under selected biological conditions the human body co-evolved to support specific microbial populations in important body locations. The living organisms that start with conception alter different parts of the body through biological changes to build an essential part of human health. The human microbiome within the body evolves continuously because of hormones changing and the combined influence of lifestyle habits diet age and genetic make-up. The changes made to the human microbiome directly affect both health and illness status **(**Whiteside SA, Razvi H, Dave S,2015)**.** Bacteria thrive in the largest number across the intestinal tract and play a key role in keeping us healthy. The body becomes at risk of mortality when microbial levels change especially during bacterial infections cancer and resistance to strong antibiotics also cardiovascular disease and inflammatory bowel disease develop **(**Pascal M, Perez-Gordo M,2018)**.**

Every human microbiome carries genetic differences shown through its individual cells. Through both natural internal processes and specific tissue responses the human genome controls about 20,000 protein-coding genes **(**Salzberg SL,2018). The human microbiome contains more coding capacity than the human genome so scientists refer to it as the "second genome" with total gene numbers that exceed human genome numbers by 100 times. Clipboard genes produce nutrients biotin vitamin B12 and folate while creating microbial life bindings and transport methods **(**Nichols RG,2021). Knowing how human microbiome biology works and how genes link with human biology is essential to understanding the relationship between bacteria and their human hosts **(**Goodrich JK, Davenport ER, Clark AG,2017)**.** Chronic health conditions such as hyperlipidemia obesity cancer and hypertension transmit from generation to generation and family members. These conditions need both genetic inheritance and dietary restrictions **(**Nichols RG,2021)**.** The study explains how the human microbiome both starts and controls diseases plus how characteristics help find which microbial genes make patients sick. We explore both present limitations and future therapy choices that researchers face when analyzing the impact of microbiome on host genetic outputs. To complete our research objective we searched 150 reviews and publications through PubMed NCBI and Google Scholar databases, and later used 65 selected studies to build this review. Our study mainly used keyword searches to collect research but left out any studies that duplicated or presented similar information.

LITERATURE REVIEW

The human microbiome consists of different physiological systems that affect health and sickness levels significantly. Dysbiosis which describes microbial imbalance in the body has demonstrated connections to obesity disorders along with autoimmune conditions and gut diseases as well as dental and skin problems. The wide range of bacteria present within the digestive tract affects how well the body defends itself from illnesses and digests food and safeguards against dangerous diseases. Understanding dysbiosis remains vital to understand disease symptoms and their inflammatory state plus treat patients effectively Metwaly A, Reitmeier S,2022). The microbiome directs disease treatment through biological methods which produce better results than medical interventions. Gastrointestinal diseases require specific therapy which includes both probiotics and fecal transplants according to medical research (Gubatan J, Boye TL,2022). The therapeutic control of illness depends heavily on the microbiome although these microorganisms start the disease path. Researchers need to study these bacteria because environmental elements can modify the human microbiome which aids treatments of gastrointestinal and human health conditions (Rengarajan S,2020). Multiple skin conditions that cause inflammation are influenced by environmental factors along with daily activities which affect the microbiome of skin tissue (Alkotob SS,2020).

The skin bacteria Staphylococcus epidermidis together with other microorganisms show reduced immune functions and inhibit host cell antimicrobial peptides according to scientific findings (Lunjani N, Ahearn-Ford S, Dube FS,2022). Food poisoning resulting from exposure to Staphylococcus aureus occurs though this bacterium works alongside other microbes to protect lactobacilli and prevent pathogen colonization (Nakatsuji T, Chen TH, Narala S, et al,2017). Human oral microbiota contains various diverse forms of bacteria together with viruses and fungal microorganisms. The microbial imbalance of the mouth leads to multiple oral human health problems including dental caries, periodontal disease and oral candidiasis (Baker JL, Mark Welch JL,2024). Systemic illnesses that include diabetes and obesity together with inflammatory bowel disease (IBD) and multiple sclerosis and rheumatoid arthritis develop from disrupted microbiota balance. The inflammatory conditions of diabetes and obesity operate to aggravate insulin resistance as well as deteriorate inflammation along with glucose metabolic processes (Pitocco D, Di Leo M, Tartaglione L, et al,2020). Human biogeography proves to be complex which leads to metabolic exchanges and host immune system activity that affect both oral and systemic health (Jaffe AL, Thomas AD, He C, et al,2021). The knowledge of systematic disease-microbiome-interaction patterns will enable medical professionals to develop unique therapeutic approaches that result in better patient health outcomes (Figure 1).

Figure 1. The role of the human microbiome in health and disease.

Factors influencing microbiome composition

The pattern of each person's microbiome depends on which organs connect to their specific route. Every part of our skin exists as a self-governing microorganism population that requires both external exposure and inner balance to remain well-balanced (Sender R, Fuchs S,2016). The effects of external factors on our microorganisms fade quickly but our mouth and stomach bacteria stay distinctive from each other. The vaginal microbiome mostly contains Lactobacillus and keeps a stable condition no matter what illness affects a person (Ravel J, Brotman RM, Gajer P, et al,2013). Our dietary choices directly change the gut microbiota and provide us a way to remake its balance. How you eat over months affects your microbiome more than short-term food changes do (David LA, Maurice CF, Carmody RN, et al,2014). The types of microorganisms that live inside you depend heavily on what you choose to do in your daily life including pet ownership. Living with pets helps lower asthma risk which means exposing ourselves to microorganisms could help rewire our immune system (Stein MM, Hrusch CL, Gozdz J, et al,2016). Light physical activity tends to modify the microbial makeup and relieves inflammation in small degrees. The links to stress and poor sleep show up as changes in gut microbiome and inflammatory system markers (Karl JP, Margolis LM, Madslien EH, et al,2017). Antibiotics affect all types of microbes strongly and especially in adult patients. Taking antibiotics at a young age may lead the body to develop IBD, obesity, and asthma as long-term health issues (Modi SR, Collins JJ,2014). Our microbiome structure differs between different body sections since several elements impact it including personal choices and medicine use. These lifestyle factors influence both body health and sickness likelihood (See Figure 2).

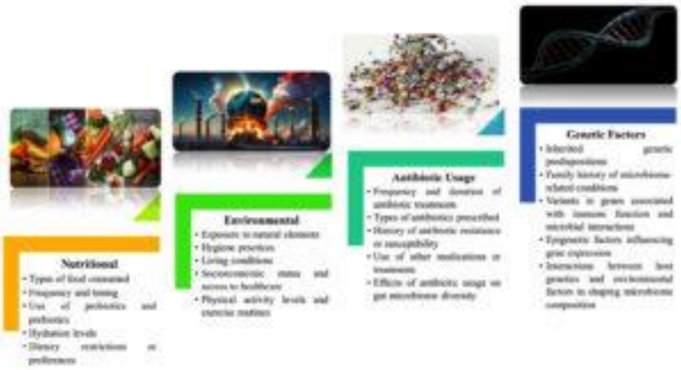

Figure 2. Factors influencing the human microbiome.

Genetic variation influences microbiome composition

The human microbiome is greatly influenced by environmental variables, but host genetics significantly influences the makeup of these microbiota. The correlation between single nucleotide polymorphisms (SNPs) and the Mediterranean fever gene (MEFV) as a result of alterations in the composition of the bacterial population in the human gut is a remarkable illustration of this interaction (Khachatryan ZA, Ktsoyan ZA,2008). There is a correlation between genes linked to IBD risk and the makeup of the gut microbiota (Li E, Hamm CM, Gulati AS, et al,2012). Mutations in the fructosyltransferase 2 gene (FUT2), which has been linked to the onset of Crohn's disease, impact energy metabolism in the gut microbiota (Tong M, McHardy I, Ruegger P, et al,2014). A higher frequency of Enterobacteriaceae species in the stomach is associated with the amount of nucleotide-binding oligomerization domain protein 2 (NOD2) alleles in individuals with IBD. Given that the human body's microbiome influences several genes, these and numerous additional interactions highlight the intricate interplay between host genetic diversity and microbial makeup. The whole host microbiome is linked to genetic variation, which impacts the gut microbiota as well. Goodrich et al studied 416 twin pairs. The impact of genetic variation on the microbiome is shown by the discovery that monozygotic twins (MZ) had more genetically identical microbial species than fraternal twins (DZ) (Goodrich JK, Waters JL, Poole AC, et al,2014). The impact of genetic diversity on the microbiota in both twin pairs was also shown by another research including monozygotic and fraternal twins and environmental variables. In order to ascertain this intricate link, mouse models have been useful. In these mouse models, quantitative trait loci (QTL) mapping has revealed a number of genes that are important for both defining the makeup of the body's microbiome and producing immunological responses.

The link between genetic variation and microbial composition has been better understood as a result of the function that host mitochondrial DNA plays in shaping the microbial community inside cells. The impact of certain microbial families, such as the Christensenaceae, on host genetic diversity was shown by Goodrich et al. However, twin studies have shown that genetic impacts are negligible in comparison to the effects of environmental variables, underscoring the significance of environmental factors in forming the host microbiome. Environmental factors also have a substantial influence on the microbial community inside the host. Additionally, microbial genomes significantly influence the microbiome's composition inside host cells and contribute to the development of the host immune system, particularly in the early stages of colonization. The manner of delivery and the mother's microbial colonization during pregnancy are the two most significant elements that affect microbial colonization of the human body. Following colonization, the microbiota produces substances such bacterial polysaccharides and flagellin that support the growth of the host immune system and preserve immunological equilibrium [35]. More precisely, these microbial communities affect many immune cell types that are critical for the growth and efficient operation of the immune system, including helper T cells, IgA-producing cells, and intraepithelial lymphocytes.

Disease management and the development of targeted treatment approaches against a range of microbial illnesses are influenced by the intricate interplay between the microbiota and host genetics, which shapes the host immune system. The genetic makeup of host cells may be significantly impacted by interactions with compounds produced by microorganisms that live in various regions of the human body as well as direct contact with these substances. An obvious example is SARS-CoV-2, which interacts with other microbes to create a variety of poisons by triggering the expression of certain genes in diverse human body areas. Intestinal samples from colonized and germ-free mice were compared using DNA microarray analysis in one research.

Genetic factors influence health outcomes

Over time pathogens and human DNA have developed together in response to widespread infectious sicknesses and health issues (Muhlemann B, Jones TC, Damgaard PdeB, et al,2018). The regular contact between microorganisms and humans changes both ancient and present human genome makeup as well as how different people inherit traits. During malaria infection Plasmodium changes the human blood cells both physically and functionally through genetic variation. Despite better diagnostic tools medical facilities keep facing outbreaks from infectious illnesses across the world. The newest example of this is COVID-19 which emerges from SARS-CoV-2. The ongoing presence of HIV, TB, hepatitis and malaria shows the direct relationship between genetic diversity and infectious diseases. Human genetic loci responsible for disease defense and DNA differences linked to infections are considered major contributors to health research. GWAS has become the accepted method to arrange these targeted areas (Muhlemann B, Jones TC, Damgaard PdeB, et al,2018). The method GWAS researchers use to study disease cases and controls does not show all the details about how diseases affect individual patients. By combining next-generation sequencing and genotyping our study will discover more about host defense against infection and how genetic differences damage the immune response to trigger infection. Multi-omics technology helps doctors recognize which genetic changes caused disease and which ones caused infections. Identifying how genes produce immunity to disease and how illness patterns affect individuals depends on studying interaction details between human genetics and pathogens to make effective treatments.

Genetic Variation and its Influence on Microbiome Composition: Insights and Implications

The human microbiome, composed of diverse microbial populations, is a crucial determinant of an individual's health and disease susceptibility. While environmental factors, such as diet, lifestyle, and exposure to pathogens, significantly shape the microbiome, genetic variation within the host also plays a vital role in influencing its composition. These interactions between host genetics and microbial communities can affect various physiological processes, leading to health outcomes and disease predisposition. This section discusses how genetic variation in the host impacts microbiome diversity, composition, and its relationship to health conditions.

Host Genetics and Microbiome Composition

The composition along with operations of the microbiome depend heavily on genetic factors in humans. Scientific research has proven the strong relationship between genetic host factors and bacterial composition in different body habitats such as the mouth and gut and skin. Studies show genetic variations among individuals link to immune response genes which impact pathogens and inflammation identification process (Rosner JL,2014). Different genetic mutations including FUT2 gene defects show evidence to modify gut microbial composition and disease susceptibility to Crohn's disease (Cho I, Blaser MJ,2012). Genetic variations in immune-related genes like NOD2 lead to higher abundance of specific microbial species within the gut according to research (Whiteside SA, Razvi H,2015). The research demonstrates reciprocal relationships because microbes change DNA variables in hosts which subsequently modulates gene expression patterns that affect disease risk. Genetic impact on microbiome variation and twin studies the composition of the microbiome receives valuable insights through research that involves twins. Scientific evidence shows that identical twins possess microbial communities which are more similar compared to fraternal twins. Scientific research indicates that the microbiota of the body has features that can be passed down through generations (Mina PR. Gut Microbiota,2023). Multiple studies demonstrate that environmental influences including nutrition and lifestyle practices substantially affect the microbiota thus proving that microbial composition results from combined genetic and environmental elements.

The composition of microbiome diversity stems from 30% to 50% environmental aspects and 30% genetic determinants based on highly detailed twin research (Hoeppli RE, Wu D, Cook L,2015). The research data shows how genetic predisposition continuously interacts with environmental exposure to determine microbiome development. Research reveals that the inheritance pattern of microbiome composition enables customized microbiome-based medical approaches which merge genetic properties within treatment strategies.

Genetic impacts on immune system development and host-microbiome interactions

The genetic composition of host organisms produces major changes in the way their immune systems perceive the microbiome. Scientific studies link modifications to the microbiome which affect immune responses to genetic differences in immune system-related genes. The presence of specific immune gene alleles like TLR (Toll-like receptors) affects body reactions to infections and chronic inflammatory diseases because their existence relates directly to changes in the gut microbiota composition (Pascal M, Perez-Gordo M, Caballero T, et al,2018). The development of the host immune system relies heavily on early microbial colonizers and both factors receive influence from genetic elements. Research shows that the first microbial population of newborns receives shape from both their mother's genes and the delivery procedure that either includes vaginal birth or surgical intervention such as cesarean section thus impacting both immune system development and later disease risk potential (Salzberg SL,2018). Scientific studies indicate that T cells and IgA-producing cells together with immune cells develop through early microbial colonization (Grice EA, Segre JA,2012).

Challenges and Limitations in Studying Microbiome–Genetics Interactions

Modern genotyping and sequencing technology now let’s scientists study entire microbial communities including full DNA data. Modern sequencing revolution allows us to count and identify every type of gut bacteria inside the human body. The two main tests used to measure microbial population levels in samples are metagenomic sequencing (MGS) and 16S rRNA gene sequencing (16S). 16S technology can precisely detect both bacterial and archaean species through highly varied sections of their bacterial 16S rRNA genes. MGS studies whole environmental genetic material to find different types of microorganisms besides bacteria such as viruses and fungi. The MGS technique gives insights into biosynthesis of xenobiotics plus helps locate gene families and resistant genes alongside transmission routes for harmful microbes. mbGWAS research continues facing challenges in obtaining precise and reliable outcomes. New DNA isolation methods that focus on 16S DNA sections and compare them to amplicon databases improve how we detect microbes. Reference-based metagenomic methods that work on any DNA source affect the reliable calculation of hereditary traits. General identification techniques show problems in bacterial studies because technology faults diminish their replication success. De novo metagenomic analysis needs large volumes of data but still provides superior detection of microbes related to various genetic markers. Basic composition studies might struggle to assemble whole genomes of rare bacteria which remains a main barrier to accurate microbe identification.

Future Research Directions and Implications for Healthcare

Scientific exploration into genetic differences in the human gut microbiota and complex human characteristics through GWAS is still in early phases of development. The study of microbiome genetics through GWAS will produce better results especially when it involves larger sample sizes and improved data sharing methods. Host-microbiome interaction research benefits most from collaborative projects and combining several studies of similar findings. While host genetics usually does not shape the gut microbiota strongly scientists can use small genetic variations of the microbiome to develop more precise personalized treatments. Screening both genetic makeup and microbiome aspects can create better personalized medical treatments by better predicting how a patient will react to medicine. Systems genetics research lets us understand the entire human genome and microbiome by combining multiple testing results from gene expression studies and other molecular investigations. Integrative technologies will make hidden connections among host healthy status and genome microbiome relationships evident. Understanding complex connections between genome and microbiome helps scientists find true disease causes and design better specific treatments for healthcare. The newly discovered links can lead doctors to better care each patient with specific treatment options.

CONCLUSION

The human microbiome uses its effects on mouth skin and stomach areas to shape health and wellness. Most health conditions start or become better through the presence of the microbiome which helps fight inflammatory and immune system functions. The environment and our everyday choices including diet, living habits and antibiotic use strongly shape our microbiome development. Our personal health results depend strongly on which microbes live in our bodies and these microorganisms develop naturally by our genetic make-up. Personalized microbiome treatments hold great promise to build better healthcare and show better results with patients. Further research combining various study types will help scientists better understand the association between host genes and digestive system bacteria. Through combined work between medical professionals and scientist's microbiome research will expand its impact on worldwide public health while being applied in medical care.

REFERENCES

Alkotob SS, Cannedy C, Harter K, et al. Advances and novel developments in environmental influences on the development of atopic diseases. Allergy. *2020;75(12):3077-3086.*

Baker JL, Mark Welch JL, Kauffman KM, McLean JS, He X. The oral microbiome: diversity, biogeography and human health. Nat Rev Microbiol. *2024;22(2):89-104.*

Cho I, Blaser MJ. The human microbiome: at the interface of health and disease. Nat Rev Genet. *2012;13(4):260-70.*

David LA, Maurice CF, Carmody RN, et al. Diet rapidly and reproducibly alters the human gut microbiome. Nature. *2014;505(7484):559-63.*

Grice EA, Segre JA. The Human Microbiome: Our Second Genome. Annu Rev Genomics Hum Genet. *2012;13:151-70.*

Goodrich JK, Davenport ER, Clark AG, Ley RE. The Relationship Between the Human Genome and Microbiome Comes into View. Annu Rev Genet. *2017;51:413-433.*

Gubatan J, Boye TL, Temby M, et al. Gut Microbiome in Inflammatory Bowel Disease: Role in Pathogenesis, Dietary Modulation, and Colitis-Associated Colon Cancer. Microorganisms. *2022;10(7):1371.*

Goodrich JK, Waters JL, Poole AC, et al. Human genetics shape the gut microbiome. Cell. *2014;159(4):789-799.*

Hoeppli RE, Wu D, Cook L, Levings MK. The environment of regulatory T cell biology: cytokines, metabolites, and the microbiome. Front Immunol. *2015;6:61.*

Jaffe AL, Thomas AD, He C, et al. Patterns of Gene Content and Co-occurrence Constrain the Evolutionary Path toward Animal Association in Candidate Phyla Radiation Bacteria. mBio. *2021;12(4):e0052121.*

Karl JP, Margolis LM, Madslien EH, et al. Changes in intestinal microbiota composition and metabolism coincide with increased intestinal permeability in young adults under prolonged physiological stress. Am J Physiol Gastrointest Liver Physiol. *2017;312(6):G559-g571.*

Khachatryan ZA, Ktsoyan ZA, Manukyan GP, Kelly D, Ghazaryan KA, Aminov RI. Predominant role of host genetics in controlling the composition of gut microbiota. PLoS One. *2008;3(8):e3064.*

Li E, Hamm CM, Gulati AS, et al. Inflammatory bowel diseases phenotype, C. difficile *and NOD2 genotype are associated with shifts in human ileum associated microbial composition.* PLoS One. *2012;7(6):e26284.*

Lunjani N, Ahearn-Ford S, Dube FS, Hlela C, O'Mahony L. Mechanisms of microbe-immune system dialogue within the skin. Genes Immun. *2021;22(5-6):276-288.*

Mina PR. Gut Microbiota: A Future Clinical Magic Bullet to Manifest Pathogenic Disease in the Current Future. J Pure Appl Microbiol. *2023;17(1):51-68.*

Metwaly A, Reitmeier S, Haller D. Microbiome risk profiles as biomarkers for inflammatory and metabolic disorders. Nat Rev Gastroenterol Hepatol. *2022;19(6):383-397.*

Modi SR, Collins JJ, Relman DA. Antibiotics and the gut microbiota. J Clin Invest. *2014;124(10):4212-4218.*

Nichols RG, Davenport ER. The relationship between the gut microbiome and host gene expression: a review. Hum Genet. *2021;140(5):747-760.*

Nakatsuji T, Chen TH, Narala S, et al. Antimicrobials from human skin commensal bacteria protect against Staphylococcus aureus *and are deficient in atopic dermatitis.* Sci Transl Med. *2017;9(378):eaah4680.*

Pascal M, Perez-Gordo M, Caballero T, et al. Microbiome and Allergic Diseases. Front Immunol. *2018;9:1584.*

Pitocco D, Di Leo M, Tartaglione L, et al. The role of gut microbiota in mediating obesity and diabetes mellitus. Eur Rev Med Pharmacol Sci. *2020;24(3):1548-1562.*

Rosner JL. Ten Times More Microbial Cells than Body Cells in Humans. Microbe Magazine. *2014;9(2):47-47.*

Rengarajan S, Vivio EE, Parkes M, et al. Dynamic immunoglobulin responses to gut bacteria during inflammatory bowel disease. Gut Microbes. *2020;11(3):405-420.*

Ravel J, Brotman RM, Gajer P, et al. Daily temporal dynamics of vaginal microbiota before, during and after episodes of bacterial vaginosis. Microbiome. *2013;1(1):29.*

Sender R, Fuchs S, Milo R. Are We Really Vastly Outnumbered? Revisiting the Ratio of Bacterial to Host Cells in Humans. Cell. *2016;164(3):337-340.*

Salzberg SL. Open questions: How many genes do we have? BMC Biol. *2018;16(1):94. https://doi.org/10.1186/s12915-018-0564-x*

Stein MM, Hrusch CL, Gozdz J, et al. Innate Immunity and Asthma Risk in Amish and Hutterite Farm Children. N Engl J Med. *2016;375(5):411-421.*

Tong M, McHardy I, Ruegger P, et al. Reprograming of gut microbiome energy metabolism by the FUT2 Crohn's disease risk polymorphism. ISME J. *2014;8(11):2193-2206.*

Whiteside SA, Razvi H, Dave S, Reid G, Burton JP. The microbiome of the urinary tract-a role beyond infection. Nat Rev Urol. *2015;12(2):81-90.*

Zhao T, Wei Y, Zhu Y, et al. Gut microbiota and rheumatoid arthritis: From pathogenesis to novel therapeutic opportunities. Front Immunol. *2022;13:1007165.*