Articles on Microbiome and MS

Sources compiled by the MS Trust

Preiningerova JL, Jiraskova Zakostelska Z, Srinivasan A, Ticha V, Kovarova I, Kleinova P, Tlaskalova-Hogenova H, Kubala Havrdova E.

Multiple Sclerosis and Microbiome.

Biomolecules. 2022 Mar 11;12(3):433. doi: 10.3390/biom12030433. PMID: 35327624; PMCID: PMC8946130.

Full text: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8946130/

Abstract

The composition of microbiota and the gut-brain axis is increasingly considered a factor in the development of various pathological conditions. The etiology of multiple sclerosis (MS), a chronic autoimmune disease affecting the CNS, is complex and interactions within the gut-brain axis may be relevant in the development and the course of MS. In this article, we focus on the relationship between gut microbiota and the pathophysiology of MS. We review the contribution of germ-free mouse studies to our understanding of MS pathology and its implications for treatment strategies to modulate the microbiome in MS. This summary highlights the need for a better understanding of the role of the microbiota in patients' responses to disease-modifying drugs in MS and disease activity overall.

Claudia Cantoni,Qingqi Lin,Yair Dorsett,Laura Ghezzi,Zhongmao Liu,Yeming Pan,Kun Chen,Yanhui Han,Zhengze Li,Hang Xiao,Matthew Gormley,Yue Liu,Suresh Bokoliya,Hunter Panier,Cassandra Suther,Emily Evans,Li Deng,Alberto Locca,Robert Mikesell et al.

Alterations of host-gut microbiome interactions in multiple sclerosis

EBioMedicine

2022 Feb;76:103798. doi: 10.1016/j.ebiom.2021.103798. Epub 2022 Jan 27.

Abstract: Background: Multiple sclerosis (MS) has a complex genetic, immune and metabolic pathophysiology. Recent studies implicated the gut microbiome in MS pathogenesis. However, interactions between the microbiome and host immune system, metabolism and diet have not been studied over time in this disorder.

Methods: We performed a six-month longitudinal multi-omics study of 49 participants (24 untreated relapse remitting MS patients and 25 age, sex, race matched healthy control individuals. Gut microbiome composition and function were characterized using 16S and metagenomic shotgun sequencing. Flow cytometry was used to characterize blood immune cell populations and cytokine profiles. Circulating

metabolites were profiled by untargeted UPLC-MS. A four-day food diary was recorded to capture the habitual dietary pattern of study participants.

Findings: Together with changes in blood immune cells, metagenomic analysis identified a number of gut microbiota decreased in MS patients compared to healthy controls, and microbiota positively or negatively correlated with degree of disability in MS patients. MS patients demonstrated perturbations of their blood metabolome, such as linoleate metabolic pathway, fatty acid biosynthesis, chalcone, dihydrochalcone, 4-nitrocatechol and methionine. Global correlations between multi-omics demonstrated a disrupted immune-microbiome relationship and a positive blood metabolome-microbiome correlation in MS. Specific feature association analysis identified a potential correlation network linking meat servings with decreased gut microbe B. thetaiotaomicron, increased Th17 cell and greater abundance of meat-associated blood metabolites. The microbiome and metabolome profiles remained stable over six months in MS and control individuals.

Full text: https://www.thelancet.com/action/showPdf?pii=S2352-3964%2821%2900592-2

Ochoa-Repáraz J, Kirby TO, Kasper LH.

The Gut Microbiome and Multiple Sclerosis.

Cold Spring Harb Perspect Med. 2018 Jun 1;8(6):a029017. doi: 10.1101/cshperspect.a029017. PMID: 29311123; PMCID: PMC5983160.

Full text: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5983160/

Abstract

The microbiome can be defined as the sum of the microbial and host's genome. Recent information regarding this complex organ suggests that in animal models of multiple sclerosis (MS), the composition of the gut microbiome can be altered, giving rise to both the effector and regulatory phases of central nervous system (CNS) demyelination. Experimental findings during the past decade in animal models of MS have provided clear evidence for the significant role of gut microbes in both the effector and regulatory phase of this condition. There is mounting evidence in preliminary human studies suggesting that a dysbiotic MS gut microbiome could affect disease progression. We propose considering the gut microbiome as a key organ for the regulation of tolerance mechanisms and speculate that the gut microbiome is the major environmental risk factor for CNS demyelinating disease. Accordingly, we hypothesize that intervention of the gut microbiome could result in safer novel therapeutic strategies to treat MS.

Boziki MK, Kesidou E, Theotokis P, Mentis AA, Karafoulidou E, Melnikov M, Sviridova A, Rogovski V, Boyko A, Grigoriadis N.

Microbiome in Multiple Sclerosis; Where Are We, What We Know and Do Not Know.

Brain Sci. 2020 Apr 14;10(4):234. doi: 10.3390/brainsci10040234. PMID: 32295236; PMCID: PMC7226078.

Full text: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7226078/

Abstract

An increase of multiple sclerosis (MS) incidence has been reported during the last decade, and this may be connected to environmental factors. This review article aims to encapsulate the current advances targeting the study of the gut-brain axis, which mediates the communication between the central nervous system and the gut microbiome. Clinical data arising from many research studies, which have assessed the effects of administered disease-modifying treatments in MS patients to the gut microbiome, are also recapitulated.

Wasko NJ, Nichols F, Clark RB.

Multiple sclerosis, the microbiome, TLR2, and the hygiene hypothesis.

Autoimmun Rev. 2020 Jan;19(1):102430. doi: 10.1016/j.autrev.2019.102430. Epub 2019 Nov 15. PMID: 31734400.

Full text:
https://www.sciencedirect.com/science/article/pii/S156899721930240X?via%3Dihub

Abstract

The pathophysiology of autoimmune diseases such as Multiple Sclerosis (MS) involves a complex interaction between genetic and environmental factors. Studies of monozygotic twins suggest a significant role for environmental factors in susceptibility to MS. Numerous studies, driven by the "Hygiene Hypothesis," have focused on the role of environmental factors in allergic and autoimmune diseases. The hygiene hypothesis postulates that individuals living in environments that are too "clean" lack the requisite exposure to "immune-tolerizing" microbial products, resulting in poorly regulated immune systems and increased immune-mediated diseases. Interestingly, few studies have linked MS with the hygiene hypothesis. Similarly, although numerous studies have examined the role of the microbiome in autoimmune diseases, there has been no consistent documentation of disease-specific alterations in the MS microbiome. In this review, we present evidence that integrating the hygiene hypothesis and the microbiome allows for the identification of novel pathophysiologic mechanisms in MS. Our central hypothesis is that the microbiome in MS represents a "defective environment" that fails to provide normal levels of "TLR2-tolerizing" bacterial products to the systemic immune system. Consistent with the hygiene hypothesis, we posit that this defective microbiome function results in abnormally regulated systemic innate immune TLR2 responses that play a critical role in both the inflammatory and defective remyelinative aspects of MS. We have completed proof of concept studies that support the inflammatory,

remyelinating, and human immune response components of this paradigm. Our studies suggest that induction of TLR2 tolerance may represent a novel approach to treating MS, inhibiting autoimmune inflammation while simultaneously facilitating remyelination.

Tankou SK, Regev K, Healy BC, Tjon E, Laghi L, Cox LM, Kivisäkk P, Pierre IV, Hrishikesh L, Gandhi R, Cook S, Glanz B, Stankiewicz J, Weiner HL.

A probiotic modulates the microbiome and immunity in multiple sclerosis.

Ann Neurol. 2018 Jun;83(6):1147-1161. doi: 10.1002/ana.25244. Epub 2018 Jun 8. PMID: 29679417; PMCID: PMC6181139.

Full text: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6181139/

Abstract

Objective: Effect of a probiotic on the gut microbiome and peripheral immune function in healthy controls and relapsing-remitting multiple sclerosis (MS) patients.

Methods: MS patients (N = 9) and controls (N = 13) were orally administered a probiotic containing Lactobacillus, Bifidobacterium, and Streptococcus twice-daily for two months. Blood and stool specimens were collected at baseline, after completion of the 2-month treatment, and 3 months after discontinuation of therapy. Frozen peripheral blood mononuclear cells (PBMCs) were used for immune cell profiling. Stool samples were used for 16S rRNA profiling and metabolomics.

Results: Probiotic administration increased the abundance of several taxa known to be depleted in MS such as Lactobacillus. We found that probiotic use decreased the abundance of taxa previously associated with dysbiosis in MS, including Akkermansia and Blautia. Predictive metagenomic analysis revealed a decrease in the abundance of several KEGG (Kyoto Encyclopedia of Genes and Genomes) pathways associated with altered gut microbiota function in MS patients, such as methane metabolism, following probiotic supplementation. At the immune level, probiotic administration induced an anti-inflammatory peripheral immune response characterized by decreased frequency of inflammatory monocytes, decreased mean fluorescence intensity (MFI) of CD80 on classical monocytes, as well as decreased human leukocyte antigen (HLA) D related MFI on dendritic cells. Probiotic administration was also associated with decreased expression of MS risk allele HLA-DQA1 in controls. Probiotic-induced increase in abundance of Lactobacillus and Bifidobacterium was associated with decreased expression of MS risk allele HLA.DPB1 in controls.

Takewaki D, Yamamura T.

Gut microbiome research in multiple sclerosis.

Neurosci Res. 2021 Jul;168:28-31. doi: 10.1016/j.neures.2021.05.001. Epub 2021 May 11. PMID: 33989681.

Full text: https://www.sciencedirect.com/science/article/abs/pii/S0168010221000973?via%3Dihub

Abstract

Recent studies identified specific gut microbial species linked to various human diseases, and gut-brain axis is currently attracting much attention in the field of microbiome science clinically and biologically. Research on multiple sclerosis (MS) and its mouse model, experimental autoimmune encephalomyelitis is one of the most active research subjects. Notably, recent achievements established the bidirectional causality between MS and gut microbiome. The reduction of gut microbiome-derived short chain fatty acids and the enrichment of gut-associated oxidative stress appear to be promoting for neurodegenerative processes. Also, researchers are trying to elucidate the mechanisms by which the microbiome regulates the onset and progression of MS. The new findings achieved by the analysis of the causal relationship between MS and the gut microbiome will provide a new therapeutic strategy for MS. These results will contribute to our understanding of the cause, prevention, and treatment of MS, and will lead to a complete cure for this disease in the future. In MS, for which no curative treatment has yet to be established, the unmet needs may be overcome through the analysis of gut microbiome.

Shahi SK, Freedman SN, Mangalam AK.

Gut microbiome in multiple sclerosis: The players involved and the roles they play.

Gut Microbes. 2017 Nov 2;8(6):607-615. doi: 10.1080/19490976.2017.1349041. Epub 2017 Aug 3. Erratum for: Addendum to: Chen J, Chia N, Kalari KR, Yao JZ, Novotna M, Soldan MM, et al. Multiple sclerosis patients have a distinct gut microbiota compared to healthy controls. Sci Rep 2016; 6:28484. PMID: 28696139; PMCID: PMC5730390.

Full text: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5730390/

Abstract

The human gut contains trillions of bacteria (microbiome) that play a major role in maintaining a healthy state for the host. Perturbation of this healthy gut microbiome might be an important environmental factor in the pathogenesis of inflammatory autoimmune diseases such as multiple sclerosis (MS). Others and we have recently reported that MS patients have gut microbial dysbiosis (altered microbiota) with the depletion of some and enrichment of other bacteria. However, the significance of gut bacteria that show lower or higher abundance in MS is unclear. The majority of gut bacteria are associated with certain metabolic pathways, which in turn help in the

maintenance of immune homeostasis of the host. Here we discuss recent MS microbiome studies and the possible mechanisms through which gut microbiome might contribute to the pathogenesis of MS.

Baecher-Allan C, Kaskow BJ, Weiner HL.

Multiple Sclerosis: Mechanisms and Immunotherapy.

Neuron. 2018 Feb 21;97(4):742-768. doi: 10.1016/j.neuron.2018.01.021. PMID: 29470968.

Full text: https://www.cell.com/neuron/fulltext/S0896-6273(18)30046-1

Abstract

Multiple sclerosis (MS) is an autoimmune disease triggered by environmental factors that act on a genetically susceptible host. It features three clinical stages: a pre-clinical stage detectable only by MRI; a relapsing-remitting (RRMS) stage characterized by episodes of neurologic dysfunction followed by resolution; and a progressive stage, which usually evolves from the relapsing stage. Advances in our understanding of the immune mechanisms that contribute to MS have led to more than ten FDA-approved immunotherapeutic drugs that target effector T cells, regulatory cells, B cells, and cell trafficking into the nervous system. However, most drugs for relapsing MS are not effective in treating progressive disease. Progressive MS features a compartmentalized immune response in the central nervous system, involving microglia cells and astrocytes, as well as immune-independent processes that drive axonal dysfunction. Major challenges for MS research involve understanding the mechanisms of disease progression, developing treatment for progressive MS, and determining the degree to which progressive disease can be prevented by early treatment. Key priorities for MS research include developing biomarkers, personalized medicine and advanced imaging, and a better understanding of the microbiome. With a better understanding of the genetic and epidemiological aspects of this disease, approaches to prevent MS are now also being considered.

Maglione A, Zuccalà M, Tosi M, Clerico M, Rolla S. Host

Genetics and Gut Microbiome: Perspectives for Multiple Sclerosis.

Genes (Basel). 2021 Jul 29;12(8):1181. doi: 10.3390/genes12081181. PMID: 34440354; PMCID: PMC8394267.

Full text: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8394267/

Abstract

As a complex disease, Multiple Sclerosis (MS)'s etiology is determined by both genetic and environmental factors. In the last decade, the gut microbiome has emerged as an important environmental factor, but its interaction with host genetics

is still unknown. In this review, we focus on these dual aspects of MS pathogenesis: we describe the current knowledge on genetic factors related to MS, based on genome-wide association studies, and then illustrate the interactions between the immune system, gut microbiome and central nervous system in MS, summarizing the evidence available from Experimental Autoimmune Encephalomyelitis mouse models and studies in patients. Finally, as the understanding of influence of host genetics on the gut microbiome composition in MS is in its infancy, we explore this issue based on the evidence currently available from other autoimmune diseases that share with MS the interplay of genetic with environmental factors (Inflammatory Bowel Disease, Rheumatoid Arthritis and Systemic Lupus Erythematosus), and discuss avenues for future research.

Esmaeil Amini M, Shomali N, Bakhshi A, Rezaei S, Hemmatzadeh M, Hosseinzadeh R, Eslami S, Babaie F, Aslani S, Torkamandi S, Mohammadi H.

Gut microbiome and multiple sclerosis: New insights and perspective.

Int Immunopharmacol. 2020 Nov;88:107024. doi: 10.1016/j.intimp.2020.107024. Epub 2020 Sep 24. PMID: 33182024.

Full text: https://pubmed.ncbi.nlm.nih.gov/33182024/

Abstract

The human gastrointestinal microbiota, also known as the gut microbiota living in the human gastrointestinal tract, has been shown to have a significant impact on several human disorders including rheumatoid arthritis, diabetes, obesity, and multiple sclerosis (MS). MS is an inflammatory disease characterized by the destruction of the spinal cord and nerve cells in the brain due to an attack of immune cells, causing a wide range of harmful symptoms related to inflammation in the central nervous system (CNS). Despite extensive studies on MS that have shown that many external and genetic factors are involved in its pathogenesis, the exact role of external factors in the pathophysiology of MS is still unclear. Recent studies on MS and experimental autoimmune encephalomyelitis (EAE), an animal model of encephalitis, have shown that intestinal microbiota may play a key role in the pathogenesis of MS. Therefore, modification of the intestinal microbiome could be a promising strategy for the future treatment of MS. In this study, the characteristics of intestinal microbiota, the relationship between intestine and brain despite the blood-brain barrier, various factors involved in intestinal microbiota modification, changes in intestinal microbial composition in MS, intestinal microbiome modification strategies, and possible use of intestinal microbiome and factors affecting it have been discussed.