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Roles of the Microbiota in the Pathogenic Mechanisms of Digestive Diseases

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Abstract

The microbiota in the host gastrointestinal tract plays key roles in metabolism, nutrient absorption, and immune regulation and is responsible for the maintenance of homeostasis. Different diseases are characterized by diverse microenvironmental properties. The specific microbiome affects the development and progression of various diseases. Dysbiosis of the microbiota contributes to the pathogenesis of diseases by promoting short-chain fatty acid production, influencing immune responses, inducing inflammatory pathways, and affecting intestinal permeability. "Molecular mimicry" is also involved in some common digestive diseases. In this review, the characteristic alterations of the microbiome in various diseases, e.g., esophageal, gastrointestinal, and liver diseases are summarized. We provide an overview of several main mechanisms by which the microbiota is linked to digestive diseases.

Keywords: Microbiota; Pathogenic mechanisms; Digestive diseases; Gastrointestinal tract

Abbreviations: SCFAs: Short-Chain Fatty Acids; PRRs: Pattern Recognition Receptors; EOE: Eosinophil Oesophagitis; TSLP: Thymic Stromal Lymphopoietin; IgA: Immunoglobulin A; GERD: Gastroesophageal Reflux Disease; Hp: Helicobacter Pylori; AIH: Autoimmune Hepatitis; PSC: Primary Sclerotic Cholangitis; PBC: Primary Biliary Cirrhosis; LPS: Lipopolysaccharides; TLR: Toll-like Receptors; NAFLD: Nonalcoholic Fatty Liver Disease; FIAF: Fasting-Induced Adipose Factor; GPCRs: G-Protein-Coupled Receptors; GLP-1: Glucagon-Like Peptide 1; AMPK: Adenosine 5′-Moophosphate-Activated Protein Kinase; HE: Hepatic Encephalopathy; AMP: Antimicrobial Peptide; CDAI: Crohn's Disease Activity Index; CD: Crohn's Disease; AIEC: Adherent-Invasive Escherichia Coli

Introduction

The massive microbiota parasitizing the normal human gastrointestinal tract maintains a balance and protects the host against illness and infection. It was previously believed that the gut microbiota in humans is established at birth. However, studies have demonstrated that microorganisms are seeded during placenta formation Rodríguez et al. [1]; Aagaard et al. [2] and are similar to the oral microenvironment, mainly including the phyla Firmicutes, Tener cutes, Proteobacteria, Bacteroidetes, and Fusobacteria Aagaard et al. [2]. Several oral bacteria are also found in the placenta, e.g., Alloprevotella rava gen. Nov. Downes et al. [3] (previously called Prevotella tannerae typically found in gingival crevices) and non-pathogenic Neisseria species Bäckhed et al. [4]. In infants, the gastrointestinal tract develops rapidly. Diet, diseases, and antibiotics can affect the microbiota. Delivery methods also have a significant influence on the microbiota; Lactobacillus are frequent in the gut of infants after vaginal delivery Avershina et al. [5] and facultative anaerobes are common after Cesarean sections Biagi et al. [6].

The fecal flora after vaginal delivery primarily represents the microenvironment of the maternal gastrointestinal tract Bäckhed et al. [4]. The gut flora is not highly diverse during the early stages of growth; two dominant phyla are Proteobacteria and Actinobacteria Rodríguez et al. [1]. In the first year, the population of microbes increases; at the age of 2.5 years, the composition and functions of microbes resemble those of adults Biagi et al. [6]. When children become adults, gut microbes stabilize. After 65 years old, Clostridium cluster IV and Bacteriaceae increase and bacterial diversity decreases Claesson et al. [7]. Accordingly, different phases of life are characterized by different dominant taxa. A variety of factors can affect the microenvironment, and disruptions in the gut microbiome are associated with a wide range of disorders. In this review, effects of microbiota on pathogenic

mechanisms in common digestive diseases are summaried and microenvironmental characters.

Physiological Effects of the Gut Microbiota on Humans

Specific microbial taxa improve intestinal epithelial cell integrity, nutrient absorption, and the regulation of the host immune system. The gut microbiota can help protect against antigen invasion. Bacteria colonizing the gut contain carbohydrate-active enzymes, which ferment carbohydrates to short-chain fatty acids (SCFAs), including butyrate, acetate, and propionate Soverini et al. [8]. The functions of SCFAs include the regulation of gene expression, cell proliferation, apoptosis, and glycolipid metabolism. Studies have also indicated that butyrate has anti-inflammatory and anti-tumor effects Morrison et al. [9]; Lin et al. [10]. As an energy source in colon cells, it can reduce bacterial translocation, thereby improving intestinal barrier function Corrêa-Oliveira et al. [11].

Additionally, the gut microbiome synthesizes vitamins that cannot be produced by humans themselves.For example, lactic acid bacteria are essential for vitamin B12 synthesis Capozzi et al. [12] and Bacillus bifidus produce folic acid Rossi et al. [13]. Bacteria in the colon metabolize bile acid to secondary bile acids, and there is a strong association between bile acid and diseases, like obesity and diabetes Palau-Rodriguez et al. [14]; Hevia et al. [15]. Therefore, the gut microbiota participates in the metabolism of various nutrients and substances related to diseases. Additionally, the microbiome maintains intestinal immune system homeostasis via interactions between pattern recognition receptors (PRRs, principally Toll-like receptors and NOD-like receptors) and microorganism-associated molecular patterns (MAMPs) Hevia et al. [15]. Accordingly, disruptions in the gut microbiome can lead to diseases or the deterioration of health, as described in the following sections.

Eosinophil oesophagitis

Eosinophil oesophagitis (EOE) is a chronic allergen-induced inflammatory disease of the esophagus. It is specifically characterized by eosinophil infiltration in the esophagus wall. EOE symptoms include dysphagia and acid reflux. Several factors influence the development of EOE. For example, it is related to environmental factors Jensen et al. [16], like living in areas of low population density Jensen et al. [16]. EOE also has a genetic component, as well. Three main genes associated with EOE have been identified to date. The thymic stromal lymphopoietin (TSLP) gene on chromosomal region 5q22 Sherrill et al. [17] is over-expressed in EOE. Similarly, CCL26 (also called eotaxin-3) Davis et al. [18] and calpain-14 are also over-expressed Davis et al. [19]. Alterations in the epithelial cell barrier Davis et al. [19] and food allergy- induced IgE cause EOE Pelz et al. [20]. Changes in the activity of the Th2-type inflammatory response also contribute to the pathogenesis of EOE Davis et al. [19]. Patients with EOE differ from healthy individuals with respect to the microbiota of the esophagus. A study by Benitez and colleagues proved that the esophageal microbiota in children with EOE is dominated by Corynebacterium and Neisseria (similar to that of the oral cavity) Benitez et al. [21].

Another study found a higher frequency of Haemophilus in the esophagus of patients with EOE than in a control group Harris et al. [22]. Proton pump inhibitors reduce Streptococcus in EOE Harris et al. [22]. The gut microbiome is related to EOE. Some specific gut bacteria, e.g., Clostridia, induce RORγt+ innate lymphoid cells and T cells that produce IL-22 Stefka et al. [23], which can decrease circulating antigens from food Stefka et al. [23]. Moreover, IL-22 promotes mucus secretion from goblet cells, with beneficial effects on the intestinal barrier Sabat et al. [24]. Clostridia can also amplify Foxp3+ Tregs and induce immunoglobulin A (IgA), which participates in adaptive mucosal immunity Atarashi et al. [25]. Thereinto Clostridia (clusters IV and XIVa) can regulate the immune response by colonic regulatory T cells Atarashi et al. [26]. However, not all Clostridia are beneficial in humans. When Clostridium difficile colonizes the intestines of infants, it can decrease the diversity of the microbiome Lee et al. [27], thereby enhancing the risk of allergic disease.

Gastroesophageal reflux disease

Gastroesophageal reflux disease (GERD) is a dysfunction in gastrointestinal motility and involves the reflux of stomach contents into the esophagus. are as follows: an excessive relaxation of the lower esophageal sphincter, a motility deficiency in the stomach or esophagus, and increased pressure of the chest and belly as a result of obesity or a high body mass index Herbella et al. [28] The microbiome of patients with GERD has specific features. A large-scale study in 2009 explored the distal esophageal mucous microbiota in the normal, GERD, and Barrett esophagus Herbella et al. [28]. GERD and Barrett esophageal tissues have high proportions of gram-negative bacteria, including Proteobacteria, Fusobacteria, Spirochaetes, and Bacteroidetes Yang et al. [29]. These microbial taxa are not definitively related to GERD. However, a common bacterium, Helicobacter pylori (Hp), can protect against GERD Howard Malnick et al. [30] and the elimination of Hp does not aggravate GERD symptoms Polat et al. [31]. The detailed mechanism underlying the role of Hp is unclear.

Autoimmune liver disease

Autoimmune liver disease includes three diseases, i.e., autoimmune hepatitis (AIH), primary sclerotic cholangitis (PSC), and primary biliary cirrhosis (PBC). AIH is characterized by damaged hepatocytes, and PSC and PBC exhibit injuries to bile duct epithelial cells. Sustained injury to the liver leads to inflammation, cell proliferation, and myoblast deposition in the portal vein. Below, we discuss the role of the gut microbiota in each of these diseases.

Autoimmune hepatitis

Bifidobacterium and Bacillus lactis has significantly decreased in the guts of patients with AIH compared with healthy individuals,

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and the bacteria /Escherichia coli ratio (B/E, representing the balance of the microbiota also decreases Lin et al. [32]. A study of AIH animal models demonstrated that the gut microenvironment of HLA-DR3 NOD mice has abundant Proteobacteria and Bacteroidetes Yuksel et al. [33]. These studies suggest that AIH involves the disruption of the intestinal microbiota in both humans and animal models. The microbiome is involved in the pathogenesis of AIH, including dysbacteriosis in the gut. The liver accepts 75% blood from the intestinal tract by enterohepatic circulation, which includes blood as well as bacteria and nutrients. Strong intestinal barrier function and detoxification are important to maintain an immune balance in the liver. Intestinal-derived toxins result in the excessive activation of the innate immune system, inducing inflammatory response signals and injuring liver tissues Yuksel et al. [33]. Analyses of lipopolysaccharides (LPS) in the plasma (an indicator of bacterial translocation) have indicated high levels in patients with AIH Lin et al. [32].

LPS is a component of the bacterial cell wall and is a type of MAMP. Toll-like receptors (TLR)are pattern-recognition receptors that recognize and combine with MAMPs, to activate the immune response. LPS interacts with LPS-binding protein (LBP) in circulation and combines with TLR4 (in the liver, TLR4 is expressed in hepatocytes) Guo et al. [34]. This process is assisted by two co-receptors, CD14 and myeloid differentiation protein 2 (MD2), and leads to the activation of the NF-dB signaling pathway. NF-dB can upregulate pro-inflammatory cytokine expression Guo et al. [34]. Accordingly, LPS-TLR4-NF-κB signaling damages liver cells and causes fibrosis. Intestinal permeability is closely related to AIH. Low levels of zonula occludens-1 (ZO-1) and occluding in descending duodenum specimens Lin et al. [32]. The disruption of tight junctions and the intestinal villus have been detected by endoscopy. The integrity of the intestinal barrier relies on the villus, tight junctions, and a balanced gut microenvironment. Decreases or disruptions in ZO-1 and Occluding weaken intestinal permeability, which may aggravate inflammation of the liver and cause AIH.

Primary biliary cirrhosis

In the bile of patients with PBC, gram-positive cocci are common in the terminal phase Mattner [35]. There is a correlation between urinary tract infection and PBC Smyk et al. [36]. Bacteriuria or urinary tract infection are involved in the PBC mechanism via cross-reactions between pyruvate dehydrogenase complex-E2(PDC-E2) of Escherichia coli and human biliary cells. This reaction is called molecular mimicry Hirschfield et al. [37]. PDC-E2 epitopes of humans are highly homologous to those of *E. coli*. An anti-mitochondrial antibody (AMA-M2) antibody is a specific serologic marker in patients with PBC, and AMA-M2 binds to PDC-E2 in the mitochondrial intimal. After infection with *E. coli* PDC-E2 of *E. coli* may interact with human tissues, cause damage Hirschfield et al. [37]. Other bacterial taxa can also cause PBC. Novosphingobium aromaticivorans induces PDC-E2 combined with the AMA-M2 reaction Mohammed et al. [38] and might be a trigger of autoimmunity in PBC (Olafsson et al.,2004). Lactobacillus Delbruck Smyk et al. [36] and Chlamydia pneumoniae Abdulkarim et al. [39] might also cause PBC by molecular mimicry. The most possible mechanism involved above microbiota is "molecular mimicry". TLR signaling by MAMPs interacting with PRRs also plays a role in the immune response in PBC Mattner [35]. TLR4 is expressed on biliary epithelial cells Wang et al. [40], and LPS (from gram-negative bacteria) is linked to the TLR4-mediated secretion of inflammatory cytokines, e.g., IL-6, IL-8, and TNF-α. Accordingly, the microbiota can destroy biliary epithelial cells Mohammed et al. [38]; Olafsson et al. [41] via chemokines.

Primary sclerotic cholangitis

The gut microbiota of patients with PSC exhibits low diversity and a low frequency of Clostridial II Rossen et al. [42]. The relationship between bile and the gut microbiota is associated with the Fructosyltransferase 2 gene (FUT2, which encodes an enzyme involved in protein glycosylation and cacodylate protein production). Its dysfunction is involved in the pathogenesis of PSC Folse Raas et al. [43] and is associated with an increase in Firmicutes in the bile acid and a decrease in microorganism diversity. Both taxonomic changes are involved in PSC Folse Raas et al. [43]. TLRs on CD11c+ dendritic cells (DCs) are activated by microbial products, like CpG DNA and peptidoglycans. This process results in IL-23 secretion, and IL-23 regulates RORγt-dependent innate lymphocytes (ILCs) Mattner [35]. ILCs produce IL-22, which up-regulates FUT2 expression Pickard et al. [44]. Cacodylate proteins (which are produced by FUT2) enter the lumen and produce SCFAs Mattner [35], which are beneficial to the bile tract environment.

These findings indicate that abnormityalities of FUT2 may contribute to PSC. As mentioned previously, Hp has a protective role in GERD. In fact, Hp can influence AIH as well. A trial by Peng et al. proved that patients with AIH who are positive for Hp have high incidences of various anti-bodies, such as AMA, ANA, SMA, ANCA, and other specific anti-bodies in AIH Peng et al. [45]. Moreover, this trial showed that high levels of IFN-γ, IL-6, IL-10, and TNF-αin AIH are associated with Hp positivity Vorobyova et al. [46]. Potential mechanisms by which Hp aggravates AIH are as follows: IFN-γ, IL-10, TNF-α, and other cytokines can damage liver cells Vorobyova et al. [46]; endotoxemia resulting from Hp can lead to inflammatory damage in liver cells Mackay et al. [47]; Hp combined with ANA forms an immune complex that can aggravate injury to the intrahepatic bile duct Peng et al. [45]; Hp releases cytotoxin associated gene A (Cagan), which enters the stomach mucosa and causes an immune response Peng et al. [45].

Nonalcoholic fatty liver disease

Nonalcoholic fatty liver disease (NAFLD) can be explained by the popular "two-hit hypothesis. "The first hit is insulin resistance (IR), which enhances the activity of liver Kupffer cells and the cells

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response to gut-derived endotoxins. The second hit is oxidative stress, resulting in ROS production, and lipid peroxidation, leading to inflammation and fibrosis Bluemel et al. [48]. The microbiome contributes to the pathogenesis of NAFLD, which is characterized by a specific microenvironment. Compared to the gut of healthy individuals, the NAFLD gut has low proportions of Bacteroidetes Mozaki et al. [49] and Ruminococcaceae Raman et al. [50]. Proteobacteria are more abundant in the gut microbiota Zhu et al. [51]. Disruptions in the intestinal flora induce NAFLD via the production of SCFAs, LPS, fasting-induced adipose factor (FIAF), and ethanol Leung et al. [52]. SCFAs generated by the microbiome activate G-protein-coupled receptors (GPCRs) on the intestinal mucosa, and the activation of GPR41 and GPR43 results in peptide YY(PYY) and glucagon-like peptide 1 (GLP-1) production Leung et al. [52]. PYY increases nutrient intake by delaying stomach emptying and intestinal peristalsis Musso et al. [53]; GLP-1 promotes insulin resistance (Vegliote-Baroni et al.,2011). These effects can aggravate NAFLD. SCFAs can also inhibit the adenosine 5′-moophosphate-activated protein kinase (AMPK) signaling pathway Den Basten et al. [54] and decrease free fatty acid β-oxidation.

Free fatty acid then accumulates in liver cells. LPS resulting from dysbacteriosis stimulates TLR4 in liver sinusoidal endothelial cells and TLR9 in dendritic cells and induces the inflammasome as well as the production of inflammatory cytokines, e.g., TNF-α and IL-1 Than et al. [55]; Federico et al. [56]. These inflammatory factors induce steatosis and fibrosis in the liver. The microbiome generates ethanol, and this endogenous ethanol destroys tight junction Leung et al. [52]. LPS and endotoxins enter the portal system more easily, destroying intestinal integrity. The intestinal flora-mediated regulation of choline metabolism influences NAFLD, as demonstrated by Dumas et al. [57]. In mice fed a high-fat diet, an imbalance in the microbiota down-regulates choline levels, which induces NAFLD Dumas et al. [57].The microbiota converts dietary lecithin to choline, and an imbalance in the flora causes low levels of very low-density lipoprotein (choline is a component of VLDL), leading to liver fat accumulation and fibrosis Wang et al. [58]. Dysbiosis also suppresses the secretion of FIAF, which can inhibit the activity of lipoprotein lipase, which can metabolize triglycerides Malaguena et al. [59]. Low levels of FIAF also activate Cheb and SREBP-1c to activate hepatic lipogenic enzymes Raman et al. [50]. Both effects enhance fat storage in the liver.

Alcoholic fatty liver

Long-term alcohol consumption leads to decreases in Bacteroidetes and Firmicutes Malaguena et al. [59] and increases in Proteobacteria and Actinobacteria Mutlu et al. [60]. Alcohol changes the balance of the microbiome; in particular, it supports the growth of Enterobacteriaceae and Proteobacteria Mutlu et al. [60]. Bacteria in the intestine convert alcohol to acetaldehyde, and dysbacteriosis increases the concentration of acetaldehyde. It leads to the redistribution of the tight junction proteins ZO-1 and occluding, and increases the permeability of the gut increase Atkinson et al. [61]. High permeability increases NF-dB and NO which induces oxidative stress Banan et al. [62]. Gram-negative bacteria that produce LPS induce the release of IL-1β and TNF by Kupffer cells, resulting in inflammation Forsyth et al. [63].

Liver cirrhosis

Liver cirrhosis is the end stage of most chronic liver diseases and has characteristic microbiome. Studies have found increased ratios of Proteobacteria, Enterobacteriaceae, Veillonellaceae, and Streptococcic (Andruzzi Zamparelli et al.,2017) and decreases in Bacteroidetes and Lachnospiraceae in the gut of patient with cirrhosis Chen et al. [64]. The flora is related to complications associated with cirrhosis, such as hepatic encephalopathy, visceral artery vasodilatation, spontaneous peritonitis, and bacteremia Gómez-Hurtado et al. [65]. Hepatic encephalopathy (HE) is a serious complication associated with ammonia. The failure of ammonia metabolism to produce urea during liver dysfunction results in its direct circulation.

The free form of ammonia can induce oxidative stress; moreover, it is converted to glutamine in brain cells. Absorbed glutamine can cause cerebral edema Gómez-Hurtado et al. [65]. Porphyromonadaceae, Alcaligene, and Enterobacteriaceae of the fecal microbiome are positively correlated with HE Bajaj et al. [66]. Alcaligene and Porphyromonadaceae metabolize urea to ammonia, leading to cognition impairment Bajaj et al. [66]. In colonic mucosal tissues, Streptococcus salivarius is elevated in patients with minimal hepatic encephalopathy, and Porphyromonadaceae is increased in overt hepatic encephalopathy Bajaj [67]. Dysbiosis decreases bacterial metabolism of bile acid. Factors such as LPS, cytokines, and ammonia will pass the blood-brain barrier. Bacterial DNA induces peritoneal macrophages to produce NO and cytokines Francés et al. [68], which can activate oxidative stress. NO also leads to visceral artery vasodilatation. Bacterial produced LPS induces TNF-α, which is involved in portal hypertension Theodorakis et al. [69]. The underlying mechanism is still not clear. Spontaneous peritonitis emerges in cirrhosis with ascites. The translocation of bacteria with weak intestinal function can cause spontaneous peritonitis's in patients with portal hypertension.

Pancreatic Disease

The role of the microbiome in pancreatic disease is still not clear. Gut microbiome translocation and endotoxins are associated with acute pancreatitis Leal-Lopes et al. [70]. Pancreas damage and the disruption of intestinal permeability result in ischemia and the excessive growth of bacteria Sharma et al. [71]. Bacteria transfer to the pancreas causes re-infection, which is main cause of death in patients with acute pancreatitis. Similarly, overgrowth of the gut microbiome occurs in chronic pancreatitis, and bacteria can influence terminal symptoms. An imbalance in the gut microbiota can cause a deficiency in Paneth cells Chen et

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al. [72], thereby decreasing antimicrobial peptide(AMP) secretion by these cells, which maintains intestinal barrier function Zhang et al. [73]. Barrier weakening leads to bacterial translocation and the aggravation of pancreatitis. Moreover, molecular mimicry is involved in autoimmune pancreatitis associated with the microbiota; commensal bacteria translocated from the gut to the pancreas can activate nucleotide-binding oligomerization domain-containing protein 1 (NOD1) in acinar cells Tsuji et al. [74]. NOD1 is a protein receptor that can combine with bacterial factors, stimulating the immune response Chen et al. [72]. Bacterial MAMPs, like LPS, interact with TLRs, resulting in the production of inflammatory cytokines, such as interferon-γ, TNF-α, IL-10, and IL-12 Nishio et al. [75]. MAMPs activate the innate immune response by combining with TLRs and nucleotide-binding domain and leucine-rich repeat-containing molecules (NLRs) induce autoimmune inflammation Tsuji et al. [74]; Werts et al. [76].

Inflammatory Bowel Disease

The diversity of the microbiota in the mucosa of patients with IBD is low Nishio et al. [75], with an altered composition. In a large-scale study of patients with IBD before treatment. Enterobacteriaceae, Fusobacteria, Pasteurellosis, and Bifidobacteria increase in IBD patients Morgan et al. [77]; Martinez-Medina et al. [78]. Microbiota may be an indicator of clinical outcomes; the Crohn's disease activity index (CDAI) is negatively related to Enterobacteriaceae Morgan et al. [79].

Crohn 's Disease

The ileal mucous membrane of Crohn's disease (CD) has high levels of adherent- invasive Escherichia coli (AIEC) Morgan et al. [79]; Martinez-Medina et al. [78]. AIEC triggers ileal inflammation and proliferation. AIEC activates the LPS-regulated inflammatory cascade reaction and influences autophagy Deering et al. [80]. Autophagic genes are essential for endothelial function Deering et al. [80]. ATG16L1 is involved in autophagy, innate immunity, and engulfing bacterial contents. AIEC down-regulates the expression of ATG16L1, and the dysfunction of autophagy occurs in CD Saraghina Sabad et al. [81]; and Salem et al. [82]. Individuals with genetic risk factors have dysfunctions in autophagy. Bacteria duplicate in macrophages and induce granuloma formation Saraghina Sabad et al. [81]. Some microbes produced SCFAs, which can be beneficial in CD. SCFAs are able to protect colon function. Faecalibacterium parasitize generates butyrate, which is lacking in patients with CD Morgan et al. [79]. F. parasitize is a therapeutic candidate; removing this bacterium enhances the risk of CD Sokol et al. [83].

Ulcerative Colonic Disease

F. parasitize is found in healthy individuals but is decreased in patients with ulcerative colonic disease (UC) Lee et al. [84]; Lopez-Siles et al. [85]. Bacteroides fragilis and Escherichia coli are enhanced in UC Kolhe et al. [86]; Nagao-Kitamoto et al. [87]. The supply of Fusicatenibacter bacterivores in patients with UC can improve colonic inflammation Takeshita et al. [88]. We discuss specific bacteria that influence UC and related mechanisms. Escherichia coli is abundant in UC, especially adherent invasive *E. coli*(AIEC), which can pass the intestinal barrier and reach deep tissues Martinez-Medina et al. [78]. AIEC invade intestinal epithelial cells. Mesalazine is an anti-inflammation drug that can relieve IBD by reducing AIEC Morgan et al. [79]. Some, but not all Bacteroides are beneficial in UC. Bacteroides fragilis can produce polysaccharide A (PSA) which converts CD4+T cells to Foxp3+ Treg cells Round et al. [89]. PSA not only interacts with TLR2 on DCs, inducing Treg cells and IL-10 expression Round et al. [89] but also prevents colonic inflammation in animal models Round et al. [89]; Zhang et al. [90]. Accordingly, B. fragilis promotes Treg cell differentiation to maintain intestinal mucous immunity. Other Bacteroides species invade and damage the gut Kuwahara et al. [91], and the gut commensal Bacteroides thetaiotaomicron can promote IBD progression Hansen et al. [92].

Infection or colonization with Hp can relieve dextran sodium sulfate-induced chronic colonic inflammation Engler et al. [93], suggesting that Hp has a protective effect dependent on the NLRP3 inflammasome and IL-18 signaling pathway Engler et al. [93]. It activates NLRP3 inflammasomes and induces autoproteolytic cleavage caspase-1 Semper et al. [94]. This process can transform pro-IL-18 to IL-18 Hitzler et al. [95]. However, some etiological data do not indicate a significant relationship between Hp and IBD Papamichael et al. [96], and the effect of Hp on IBD is still controversial.Faecalibacterium prausnitzii protects the colon by generating SCFAs, which induce Treg cells, supply energy to endothelial cells of the gut, up-regulate the secretion of IL-10, and disrupt NF-κB activation to prevent IL-8 production Sarrabayrose et al. [97]; Ohkusa et al. [98] Some Clostridium species related to UC include C. difficile, C. coccoides, and C. leptum Kolho et al. [86]. C. difficile secretes endotoxins that injure the intestinal barrier Young et al. [99]. C. coccoides (also called Clostridium cluster XIVa) and C. leptum (also called Clostridium cluster IV) are associated with UC. Both bacteria produce butyrate to maintain gut integrity Louis et al. [100] and reduce the incidence of UC. Clostridium cluster IV induces Treg cell and DC production and stimulates DCs to increase Treg cells Li et al. [101]. It reduces the immune inflammatory response by decreasing T helper cells (Th1, Th2, and Th17) Li et al. [101].

Conclusion

The gut microbiome protects against the pathologic mechanisms of digestive diseases by producing beneficial substances, like IgA and SCFAs (except in NAFLD) Moore et al. [102]. Dysbiosis can induce the NF-κB pathway or inflammatory cytokines, which can cause inflammatory injury to tissues [103]. Additionally, some specific microbiota maintain immune

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homeostasis by regulating immune cells, like Treg cells. Molecular mimicry is one of the main factors in some autoimmune diseases, like PBC. The microbiota influences tight junctions, thereby enhancing or weakening intestinal permeability [104-106]. It is involved in common digestive diseases, and other underlying genetic factors and microbiota-derived metabolites are not fully described in this review. Furthermore, this article does not consider all types of microbiotas (e.g., fungi parasites, and viruses are not included); the mechanisms described here are specifically related to bacteria. Further studies are needed to clarify the roles of other types of microbiotas. Finally, understanding the effects of bacteria on diseases may guide treatment and prevention. Detailed treatment strategies related to the microbiota are outside the scope of this review. However, many studies have shown that probiotics, or the avoidance of intestinal microflora disorders can effectively treat or prevent diseases.

References

1. Rodríguez JM, Murphy K, Stanton C, Ross RP, Kober OI, et al. (2015) The composition of the gut microbiota throughout life, with an emphasis on early life. Microb Ecol Health Dis 26: 26050.
2. Aagaard K, Ma J, Antony KM, Ganu R, Petrosino J (2014) The placenta harbors a unique microbiome. Sci Transl Med 6(237): 237ra65.
3. Downes J, Dewhirst FE, Tanner A, Wade WG (1994) Description of Alloprevotella rava gen nov sp Nov isolated from the human oral cavity, and reclassification of Prevotella tannerae as Alloprevotella tannerae. Int J Syst Evol Microbiol 63(Pt4): 1214-1218.
4. Bäckhed F, Roswall J, Peng Y, Feng Q, Jia H (2015) Dynamics and stabilization of the Human Gut Microbiome during the First Year of Life. Cell Host Microbe 17(5): 690-703.
5. Avershina E, Storrø O, Øien T, Johnsen R, Pope P (2014) Major faecal microbiota shifts in composition and diversity with age in a geographically restricted cohort of mothers and their children. FEMS Microbiol Ecol 87(1): 280-290.
6. Biagi E, Nylund L, Candela M, Ostan R, Bucci L (2010) Through ageing and beyond: gut microbiota and inflammatory status in seniors and centenarians. PLoS One 5(5): e10667.
7. Claesson J, Cusack S, O'Sullivan O, Greene-Diniz R, De Weerd, et al. (2011) Composition, variability, and temporal stability of the intestinal microbiota of the elderly. Proc Natl Acad Sci 108(Suppl1): 4586-4591.
8. Soverini M, Turroni S, Biagi E, Quercia S, Brigidi P, et al. (2017) Variation of Carbohydrate- Active Enzyme Patterns in the Gut Microbiota of Italian Healthy Subjects and Type 2 Diabetes Patients. Front Microbiol 8: 2079.
9. Morrison DJ, Preston T (2016) Formation of short chain fatty acids by the gut microbiota and their impact on human metabolism. Gut Microbes 7(3): 189-200.
10. Lin L, Zhang JQ (2017) Role of intestinal microbiota and metabolites on gut homeostasis and human diseases. BMC Immunol 18(1): 2.
11. Corrêa-Oliveira R, Fachi JL, Vieira A, Sato FT, Vinolo MA (2016) Regulation of immune cell function by short-chain fatty acids. Clin Transl Immunology 5(4): e73.
12. Capozzi V, Russo P, Dueñas MT, López P, Spano G (2012) Lactic acid bacteria producing B-group Vitamins: A great potential for functional cereals products. Appl Microbiol Biotechnol 96(6): 1383-1394.
13. Rossi M, Amaretti A, Raimondi S (2011) Folate production by probiotic bacteria. Nutrients 3(1): 118-134.
14. Palau-Rodriguez M, Tulipani S, Isabel Queipo-Ortuño M, Urpi-Sarda M, Tinahones FJ, et al. (2015) Metabolomic insights into the intricate gut microbial-host interaction in the development of obesity and type 2 diabetes. Front Microbiol 6: 1151.
15. Hevia A, Delgado S, Sánchez B, Margolles A (1985) Molecular players involved in the interaction between beneficial bacteria and the immune. Front Microbiol 6:1151.
16. Jensen ET, Hoffman K, Shaheen NJ, Genta RM, Dellon ES (2014) Esophageal eosinophilia is increased in rural areas with low population density: results from a national pathology database. Am J Gastroenterol 109(5): 668-675.
17. Sherrill JD, Gao PS, Stucke EM, Blanchard C, Collins MH, et al. Variants of thymic stromal lymphopoietin and its receptor associate with eosinophilic esophagitis. J Allergy Clin Immunol 26(1): 160-165.
18. Davis BP, Rothenberg ME (2016) Mechanisms of Disease of Eosinophilic Esophagitis. Annu Rev Pathol 11: 365-393.
19. Davis BP, Stucke EM, Khorki ME, Litosh VA, Rymer JK, et al. (2016) Eosinophilic esophagitis-linked calpain 14 is an IL-13-induced protease that mediates esophageal epithelial barrier impairment. JCI Insight 4: e86355.
20. Pelz BJ, Wechsler JB, Amsden K, Singh AM, Wershil BK, et al. (2016) IgE-associated food allergy alters the presentation of pediatric eosinophilic esophagitis. Clin Exp Allergy 46(11): 1431-1440.
21. Benitez AJ, Hoffmann C, Muir AB, Dods KK, Spergel JM (2015) Inflammation-associated microbiota in pediatric eosinophilic esophagitis. Microbiome 3: 23.
22. Harris JK, Fang R, Wagner BD, Choe HN, Kelly CJ (2015) Esophageal microbiome in eosinophilic esophagitis. PloS One 10(5): e0128346.
23. Stefka AT, Feehley T, Tripathi P, Qiu J, McCoy K, et al. (2014) Commensal bacteria protect against food allergen sensitization. Proc Natl Acad Sci USA 111(36): 13145 -13150.
24. Sabat R, Ouyang W, Wolk K (2014) Therapeutic opportunities of theIL-22-IL-22R1 system. Nat Rev Drug Discov 13(1): 21-38.
25. Atarashi K, Tanoue T, Oshima K, Suda W, Nagano Y, et al. (2013) Treg induction by a rationally selected mixture of Clostridia strains from the human microbiota. Nature 500(7461): 232-236.
26. Atarashi K, Tanoue T, Shima T, Imaoka A, Kuwahara T (2011) Induction of colonic regulatory T cells by indigenous Clostridium species. Science 331(6015): 337-341.
27. Lee SH, Gong YN, Ryoo E (2017) Clostridium difficile colonization and/or infection during infancy and the risk of childhood allergic diseases. Korean J Pediatr 60(5): 145–150.
28. Herbella FA, Patti MG (2010) Gastroesophageal reflux disease: from pathophysiology to treatment. World J Gastroenterol 16(30): 3745-3749.
29. Yang L, Lu X, Nossa CW, Francois F, Peek RM, et al. (2009) Inflammation and intestinal metaplasia of the distal esophagus are associated with alterations in the microbiome. Gastroenterology 137(2): 588-597.
30. Howard Malnick SD, Melzer E, Attali M, Duek G, Yahav J (2014) Helicobacter pylori: Friend or foe? World J Gastroenterol 20(27): 8979-8985.
31. Polat FR, Polat S (2012) The Effect of Helicobacter Pylori on Gastroesophageal Reflux Disease. JSLS 16(2): 260-263.

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32. Lin R, Zhou L, Wang B (2015) Abnormal intestinal permeability and microbiota in patients with autoimmune hepatitis. Int J Clin Exp Pathol 8(5): 5153-5160.

33. Yuksel M, Wang Y, Tai N, Peng J, Guo J, et al. (2015) A novel "humanized mouse" model for autoimmune hepatitis and the association of gut microbiota with liver inflammation. Hepatology 62(5): 1536-1550.

34. Guo J, Friedman SL (2010) Toll-like receptor 4 signaling in liver injury and Hepatic fibrogenesis. Fibrogenesis Tissue Repair 3: 21.

35. Mattner J (2016) Impact of Microbes on the Pathogenesis of Primary Biliary Cirrhosis (PBC) and Primary Sclerosing Cholangitis (PSC).Int J Mol Sci 17(11): 1864.

36. Smyk DS, Bogdanos DP, Kriese S, Billinis C, Burroughs AK, et al. (2012) Urinary tract infection as a risk factor for autoimmune liver disease: From bench to bedside. Clinics and Research in Hepatology and Gastroenterology 36(2): 110-121.

37. Hischfield GM, Gershwin ME (2013) The immunobiology and pathophysiology of primary biliary cirrhosis. Annu Rev Pathol 8: 303-330.

38. Mohammed JP, Fusakio ME, Rainbow DB, Moule C, Fraser HI, et al. (2011) Identification of Cd101 as susceptibility gene for Novosphingobium aromaticivorans-induced liver autoimmunity. J Immunol 187(1): 337-349.

39. Abdulkarim AS, Petrovic LM, Kim WR, Angulo P, Lloyd RV (2003) Primary biliary cirrhosis: An infectious disease caused by Chlamydia pneumoniae? J Hepatol 40: 380-384.

40. Wang AP, Migita K, Ito M, Takii Y, Daikoku M, et al. (2005) Hepatic expression of toll-like receptor 4 in primary biliary cirrhosis. J Autoimmun 25(1): 85 -91.

41. Olafsson S, Gudjonsson H, Selmi C, Amano K, Invernizzi P, et al. (2004) Antimitochondrial antibodies and reactiveity to N.aromaticivorans proteins in Icelandic patients with primary biliary cirrhosis and their relatives. Am J Gastroenterol 99(11): 2143-2146.

42. Rossen NG, Fuentes S, Boonstra K, D'Haens GR, Heilig HG, et al. (2015) The mucosa- associated microbiota of PSC patients is characterized by low diversity and low abundance of uncultured Clostridiales II. J Crohns Colitis 9(4): 342-348.

43. Folseraas T, Melum E, Rausch P, Juran BD, Ellinghaus E (2012) Extended analysis of a genome-wide association study in primary sclerosing cholangitis detects multiple novel risk loci. J Hepatol 57(2): 366-375.

44. Pickard JM, Maurice CF, Kinnebrew MA, Abt MC, Schenten D, et al. (2014) Rapid fucosylation of intestinal epithelium sustains host-commensal symbiosis in sickness. Nature 514(7524): 638-641.

45. Peng XG, Li YY, Chen HT, Zhou Y, Ma JG (2017) Evolution of correlation between Helicobacter pylori infection and autoimmune liver disease. Exp Ther Med 14(2): 1487-1490.

46. Vorobjova T, Nilsson I, Terjajev S, Granholm M, Porkka T, et al. (2006) Serum antibodies to enterohepatic Helicobacter spp.in patients with chronic liver diseases and in a population with high prevalence of H. pylori infection. Dig Liver Dis 38(3): 171-176.

47. Mackay IR, Leskovsek NV, Rose NR (2008) Cell damage and autoimmunity: A critical appraisal. J Autoimmun 30(1-2): 5-11.

48. Bluemel S, Williams B, Knight R, Schnabl B (2016) Precision medicine in alcoholic and nonalcoholic fatty liver disease via modulating the gut microbiota. Am J Physiol Gastrointest Liver Physiol 311(6): G1018-G1036.

49. Mouzaki M, Comelli EM, Arendt BM, Bonengel J, Fung SK, et al. (2013) Intestinal Microbiota in patients with nonalcoholic fatty liver disease. Hepatology 58(1): 120-127.

50. Raman M, Ahmed I, Gillevet PM, Probert CS, Ratcliffe NM, et al. (2013) Fecal microbiome and volatile organic compound metabolome in obese humans with nonalcoholic fatty liver disease. Clin Gastroenterol Hepatol 11(7): 868-875.

51. Zhu L, Baker SS, Gill C, Liu W, Alkhouri R, et al. (2013) Characterization of gut microbiomes in nonalcoholic steatohepatitis (NASH)patients: a connection between endogenous alcohol and NASH. Hepatology 57(2): 601-609.

52. Leung C, Rivera L, Furness JB, Angus PW (2016) The role of the gut microbiota in NAFLD. Nat Rev Gastroenterol Hepatol 13(7): 412-425.

53. Musso G, Gambino R, Cassader M (2010) Obesity, diabetes, and gut microbiota: the hygiene hypothesis expanded? Diabetes Care 33(10): 2277-2284.

54. Den Besten G, Bleeker A, Gerding A, Van Eunen, K, Having R (2013) Short-chain fatty acids protect against high-fat diet-induced obesity via a PPARγ-dependent switch from lipogenesis to fat oxidation. Diabetes 64(7): 2398-2408.

55. Than NN, Newsome PN (2015) A concise review of non-alcoholic fatty liver disease. Atherosclerosis 239(1): 192-202.

56. Federico A, Dallio M, Godos J, Loguercio C, Salomone E, et al. (2016) Targeting gut-liver axis for the treatment of nonalcoholic steatohepatitis: translational and clinical evidence. Transl Res 167(1): 116-124.

57. Dumas ME, Barton RH, Toye A, Cloarec O, Blancher C (2006) Metabolic profiling reveals a contribution of gut microbiota to fatty liver phenotype in insulin-resistant mice. Proc Natl Acad Sci USA 103(33): 12511-12516.

58. Wang Z, Klipfell E, Bennett BJ, Koeth R, Levison BS, et al. (2011) Gut flora metabolism of phosphatidyl-choline promotes cardiovascular disease. Nature 472(7341): 57-63.

59. Malaguarnera G, Giordano M, Nunnari G, Bertino G, Malaguarnera M, et al. (2014) Gut microbiota in alcoholic liver disease: Pathogenetic role andtherapeutic perspectives. World J Gastroenterol 20(44): 16639-16648.

60. Mutlu EA, Gillevet PM, Rangwala H, Sikaroodi M, Naqvi A, et al. (2012) Colonic Microbiome is altered in alcoholism. Am J Physiol Gastrointest Liver Physiol 302(9): G966-G978.

61. Atkinson KJ, Rao RK (2001) Role of protein tyrosine phosphorylation in acetaldehyde-Induced disruption of epithelial tight junctions. Am J Physiol Gastrointest Liver Physiol 80(6): G1280-G1288.

62. Banan A, Keshavarzian A, Zhang L, Shaikh M, Forsyth CB, et al. (2007) NF-kappa B activation as a key mechanism in ethanol-induced disruption of the Fact in cytoskeleton and monolayer barrier integrity in intestinal epithelium. Alcohol 41(6): 447-460.

63. Forsyth CB, Farhadi A, Jakate SM, Tang Y, Shaikh M (2008) Lactobacillus GG treatment ameliorates alcohol-induced intestinal oxidative stress, gut leakiness, and liver injury in a rat model of alcoholic steatohepatitis. Alcohol 43(2): 163-172.

64. Chen Y, Yang F, Lu H, Wang B, Chen Y (2011) Characterization of fecal microbial communities in patients with liver cirrhosis. Hepatology 54(2): 562-572.

65. Gómez-Hurtado I, Such J, Sanz Y, Francés R (2020) Gut microbiota-related complications in cirrhosis. World J Gastroenterol 20(45):16795-16810.

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66. Bajaj JS, Ridlon JM, Hylemon PB, Thacker LR, Heuman DM (2012) Linkage of gut microbiome with cognition in hepatic encephalopathy. Am J Physiol Gastrointest Liver Physiol 302(1): G168-G175.

67. Bajaj JS (2014) The role of microbiota in hepatic encephalopathy. Gut Microbes 5(3): 397-403.

68. Francés R, Muñoz C, Zapater P, Uceda F, Pascual S (2003) Bacterial DNA activates cell mediated immune response and nitric oxide overproduction in peritoneal macrophages from patients with cirrhosis and ascites. Gut 53(6): 860-864.

69. Theodorakis NG, Wang YN, Maluccio MA, Skill NJ (2010) Tumor necrosis factor alpha signaling in the development of experimental murine pre-hepatic portal hypertension. Int JPhysiol Pathophysiol Pharmacol 2(2): 104-110.

70. Leal LC, Velloso FJ, Campopiano JC, Sogaya MC, Correa RG (2015) Roles of commensal microbiota in Pancreas Homeostasis and Pancreatic Pathologies. J Diabetes Res 2015: 284680.

71. Sharma M, Sachdev V, Singh N, Bhardwaj P, Pal A, et al. (2012) Alterations in intestinal permeability and endotoxemia in severe acute pancreatitis. Trop Gastroenterol 33(1): 45-50.

72. Chen J, Huagn C, Wang J, Zhou H, Lu Y (2017) Dysbiosis of intestinal Microbiota and decrease in Paneth cell antimicrobial peptide level during acute necrotizing pancreatitis in rats. PLoS One 12(4): e0176583.

73. Zhang Z, Liu Z (2016) Paneth cells: The hub for sensing and regulating intestinal flora. Sci China Life Sci 59(5): 463 -467.

74. Tsuji Y, Watanabe T, Kudo M, Arai H, Strober W, et al. (2012) Sensing of commensal Organisms by the intracellular sensor nod1 mediates experimental pancreatitis. Immunity 37(2): 326-338.

75. Nishio A, Asada M, Uchida K, Fukui T, Chiba T, et al. (2011) The role of innate immunity in the pathogenesis of experimental autoimmune pancreatitis in mice. Pancreas 40(1): 95-102.

76. Werts C, Rubino S, Ling A, Girardin SE, Philpott DJ, et al. (2011) Nod-like receptors in intestinal homeostasis, inflammation, and cancer. J Leukoc Biol 90(3): 471-482.

77. Morgan XC, Tickle TL, Sokol H, Gevers D, Devaney KL, et al. (2012) Dysfunction of the intestinal microbiome in inflammatory bowel disease and treatment. Genome Biol 13(9): R79.

78. Martinez-Medina M, Aldeguer X, Lopez-Siles M, González-Huix F, López-Oliu C, et al. (2009) Molecular diversity of Escherichia coli in the human gut: new ecological evidence supporting the role of adherent-invasive E. coli (AIEC) in Crohn's disease. Inflamm Bowel Dis 15(6): 872-882.

79. Morgan XC, Tickle TL, Sokol H, Gevers D, Devaney KL, et al. (2012) Dysfunction of the intestinal microbiome in inflammatory bowel disease and treatment. Genome Biol 13(9): R79.

80. Deuring JJ, Fuhler GM, Konstantinov SR, Peppelenbosch MP, Kuipers EJ (2014) Genomic ATG_16L_1 risk allele-restricted Paneth cell ER stress in quiescent Crohn's disease. Gut 63(7):1081-1091.

81. Sadaghian Sabad M, Regeling A, deGoffau MC, Blokzijl T, Weers, et al. (2015) The ATG16L1-T300A allele impairs clearance of pathosymbionts in the inflamed ileal mucosa of Crohn's disease patients. Gut 4(10): 1546-1552.

82. Salem M, Ammitzboell M, Nys KN, S eidelin JB, Nielsen OH, et al. (2015) ATG16L1: A multifunctional susceptibility factor in Crohn disease. Autophagy 11(4): 585-594.

83. Sokol H, Pigneur B, Watterlot L, Lakhdari O, Bermúdez-Humarán, et al. (2008) Faecalibacterium prausnitzii is an anti-inflammatory commensal bacterium identified by gut microbiota analysis of Crohn disease patients. Proc Natl Acad Sci U S A 105(43): 16731-1676.

84. Lee T, Clavel T, Smirnov K, Schmidt A, Lagkouvardos I (2017) Oral versus intravenous iron replacement therapy distinctly alters the gut microbiota and metabolome in patients with IBD. Gut 66(5): 863-871.

85. Lopez-Siles M, Duncan SH, Garcia Gil LJ, Martinez-Medina M (2017) Faecalibacterium prausnitzii: from microbiology to diagnostics and prognostics. ISMEJ 11(4): 841-852.

86. Kolho KL, Korpela K, Jaakkola T, Pichai MV, Zoetendal EG (2015) Fecal Microbiota in Pediatric Inflammatory Bowel Disease and Its Relation to Inflammation. Am J Gastroenterol 110(6): 921-930.

87. Nagao-Kitamoto H, Shreiner AB, Gillilland MG, Kitamoto S, Ishii C, et al. (2016) Functional Characterization of Inflammatory Bowel Disease-Associated Gut Dysbiosis in Gnotobiotic Mice. Cell Mol Gastroenterol Hepatol 2(4): 468-481.

88. Takeshita K, Mizuno S, Mikami Y, Sujino T, Saigusa K, et al. (2016) A Single Species of Clostridium Subcluster XIVa Decreased in Ulcerative Colitis Patients. Inflamm Bowel Dis 22(12): 2802-2810.

89. Round JL, Mazmanian SK (2010) Inducible Foxp3+ regulatory T-cell development by a commensal bacterium of the intestinal microbiota. Proc Natl Acad Sci USA 107(27): 12204 -12209.

90. Zhang SL, Wang SN, Miao CY (2017) Intestinal Immune System in Ulcerative Colitis and Its Intervention. Front Immunol 8: 1674.

91. Kuwahara T, Yamashita A, Hirakawa H, Nakayama H, Toh H (2004) Genomic analysis of Bacteroides fragilis reveals extensive DNA inversions regulating cell surface adaptation. Proc Natl Acad Sci USA 101(41): 14919-14924.

92. Hansen JJ, Huang Y, Goeser L, Fan TJ, Chang EB (2012) The colitis-associated transcriptional profile of commensal Bacteroides the taiotaomicron enhances Adaptive immune responses to a bacterial antigen. PLoS One 7(8): e42645.

93. Engler DB, Leonardi I, Hartung ML, Kyburz A, Spath S (2017) Helicobacter pylori specific protection against inflammatory bowel disease requires the NLRP3 inflammasome and IL-18. Inflamm Bowel Dis 1(4): 854-861.

94. Semper RP, Mejías-Luque R, Gro C, Anderl F, Müller A, et al. (2014) Helicobacter pylori-Induced IL-1 beta secretion in innate immune cells is Regulated by the NLRP3 inflammasome and requires the Cag pathogenicity island. J Immunol 193(7): 3566-3576.

95. Hitzler I, Sayi A, Kohler E, Engler DB, Koch KN (2012) Caspase-1 has both proinflammatory and regulatory properties in Helicobacter infections, which are differentially mediated by its substrates IL-1beta and IL-18. J Immunol 188: 3594-3602.

96. Papamichael K, Konstantopoulos P, Mantzaris GJ (2014) Helicobacter pylori infection and inflammatory bowel disease: is there a link? World J Gastroenterol 20(21): 6374-6385.

97. Sarrabayrose G, Bossard C, Chauvin JM, Jarry A, Meurette G, et al. (2014) CD4CD8αα lymphocytes, a novel human regulatory T cell subset induced by colonic bacteria and deficient in patients with inflammatory bowel disease. PLoS Biol 12(4): e1001833.

98. Ohkusa T, Koido S (2015) Intestinal microbiota and ulcerative colitis. J Infect Chemother 21(11): 761-768.

99. Young VB, Hanna PC (2014) Overlapping roles for toxins in Clostridium difficile infection. J Infect Dis 209(1): 9-11.

100. Louis P, Flint HJ (2009) Diversity, metabolism and microbial ecology of butyrate-producing bacteria from the human large intestine. FEMS Microbiol Lett 294(1): 1-8.

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101. Li YN, Huang F, Cheng HJ, Li SY, Liu L, et al. (2014) Intestine-derived Clostridium leptum induces murine tolerogenic dendritic cells and regulatory T cells in vitro. Hum Immunol 75(12): 1232-1238.

102. Moore LV, Johnson JL, Monoreme (1994) Descriptions of Prevotella tannerae sp. nov. and Prevotella enoteca spinor. from the human gingival crevice and emendation of the description of Prevotella zoogleoformans. Int J Syst Bacteriol 44(4): 599-602.

103. Martinez-Medina M, Garcia-Gil LJ (2014) Escherichia coli in chronic inflammatory bowel diseases: an update on adherent invasive Escherichia coli pathogenicity. World J Gastrointest Pathophysiol 5(3): 213-227.

104. Mattner J (2016) Impact of Microbes on the Pathogenesis of Primary Biliary Cirrhosis (PBC) and Primary Sclerosing Cholangitis (PSC). Int J Mol Sci 17(11): 1864.

105. Svegliati-Baroni G, Saccomanno S, Rychlicki C, Agostinelli L, De MinicisS, et al. (2011) Glucagon-like peptide-1 receptor activation stimulates hepatic lipid oxidation and restores hepatic signalling alteration induced by a high-fat diet in nonalcoholic steatohepatitis. Liver Int 31(9): 1285-1297.

106. Sanduzzi Zamparelli M, Rocco A, Compare D, Nardone G (2017) The gut microbiota: A new potential driving force in liver cirrhosis and hepatocellular carcinoma. United European Gastroenterol J 5(7): 944-953.

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