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Contents

Weekly Volume 30 Number 15 April 21, 2024

EDITORIAL

MINIREVIEWS

ORIGINAL ARTICLE

Case Control Study

Retrospective Study

Basic Study

LETTER TO THE EDITOR

World Journal of Gastroenterology

Weekly Volume 30 Number 15 April 21, 2024

Contents

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EDITORIAL

Probiotics: Shaping the gut immunological responses

Eirini Filidou, Leonidas Kandilogiannakis, Anne Shrewsbury, George Kolios, Katerina Kotzampassi

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Abstract

Probiotics are live microorganisms exerting beneficial effects on the host's health when administered in adequate amounts. Among the most popular and adequately studied probiotics are bacteria from the families *Lactobacillaceae*, *Bifidobacteriaceae* and yeasts. Most of them have been shown, both *in vitro* and *in vivo* studies of intestinal inflammation models, to provide favorable results by means of improving the gut microbiota composition, promoting the wound healing process and shaping the immunological responses. Chronic intestinal conditions, such as inflammatory bowel diseases (IBD), are characterized by an imbalance in microbiota composition, with decreased diversity, and by relapsing and persisting inflammation, which may lead to mucosal damage. Although the results of the clinical studies investigating the effect of probiotics on patients with IBD are still controversial, it is without doubt that these microorganisms and their metabolites, now named postbiotics, have a positive influence on both the host's microbiota and the immune system, and ultimately alter the topical tissue microenvironment. This influence is achieved through three axes: (1) By displacement of potential pathogens *via* competitive exclusion; (2) by offering protection to the host through the secretion of various defensive mediators; and (3) by supplying the host with essential nutrients. We will analyze and discuss almost all the *in vitro* and *in vivo* studies of the past 2 years dealing with the possible favorable effects of certain probiotic genus on gut immunological responses, highlighting which species are the most beneficial against intestinal inflammation.

Key Words: Probiotics; Lactobacillaceae; Bifidobacteriaceae; Saccharomyces; Intestinal inflammation; Immune responses

Core Tip: Probiotics, such as *Lactiplantibacillus plantarum* and *Saccharomyces cerevisiae*, exert remarkable anti-inflammatory properties on the gut's immune responses. These beneficial microorganisms not only restore immunity markers but also enrich the gut's microbiota, crucial for a healthy microbial balance. Incorporating probiotics or foods rich in these beneficial microorganisms, particularly in conditions such as inflammatory bowel disease, holds promise for restoring gut health, boosting the immune system, and alleviating inflammation.

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INTRODUCTION

According to the current definition, "probiotics are live microorganisms that, when administered in adequate amounts, confer a health effect on the host"[1,2]. They can be found either as pure forms supplied by various pharmaceutical companies or as essential parts of everyday foods, mainly fermented, such as cheese, yogurt, beer and others[3]. Some of the most well-studied probiotics are bacteria, such as the *Lactiplantibacillus plantarum*, and yeasts, such as *Saccharomyces*, for which extensive research has shown that they possess anti-inflammatory and wound healing properties[4,5].

Probiotics are considered to exert their beneficial effects not only on the host's cells, but also on its natural microbiota composition. Since the onset of the Microbiome Project, several species of bacteria and yeasts have been identified, which has led to the extensive identification/characterization, of the human microbiota composition, found on the cutaneous and mucus surfaces of the human body[6]. Microbiota has been proved to be essential for the host's survival, not only acting as a defense mechanism against potential pathogenic microorganisms, but also providing viable nutritional supplementation[7]. Over time, it has been shown that the microbiota population is 10 times greater than the total number of cells composing the human body, and, as a result, it has been proposed that humans are "symbiotic" organisms, living in harmony with their microbiota[8].

One of the mucosal surfaces with the best characterized and most well-studied microbiota is that of the intestine. Under healthy conditions, the composition of the intestinal microbiota is balanced and beneficial to the host, but in pathological situations, this balance can be disturbed, leading to dysbiosis, with potentially harmful consequences to the host[9]. Such a dysbiosis has been confirmed in patients suffering from inflammatory bowel disease (IBD)[9]. IBDs – Crohn's Disease (CD) and Ulcerative Colitis (UC) – are characterized by chronic relapsing inflammation of the gastrointestinal tract, with various immunological, genetic and environmental factors involved in its pathogenesis[9]. One such environmental factor is the intestinal microbiota. Patients with IBDs have been shown to have a distinct, altered microbiota composition, lower in diversity compared to healthy individuals, and, in many cases, attempts to restore their microbiota composition to a healthy state have proved beneficial for the patient's health. Such attempts have been through either fecal microbial transplantation, where fecal matter from healthy donors is transplanted into patients with IBD to restore their microbiota to a healthy state, or through probiotic supplementation[10].

One of the major beneficial effects of probiotics is their ability to modulate the immunological responses of the host. This can be accomplished by: (1) Displacement of potential pathogens *via* competitive exclusion; (2) offering protection to the host through the secretion of various defensive mediators; and (3) supplying the host with essential nutrients[7]. In this Editorial, we will analyze and discuss almost all the *in vitro* and *in vivo* studies published on the past 2 years which have investigated the possible favorable effects of certain genus of probiotics on gut immunological responses (Figure 1), in an effort to highlight which are the most beneficial in relation to intestinal inflammation.

THE GENUS LACTIPLANTIBACILLUS

Lactiplantibacillus (formerly known as *Lactobacillus*), is a genus of Gram-positive bacteria that has been associated with favorable outcomes for the host. Many of its members have been proved to be essential players in the food industry[11]. One of the most well-known is *Lactiplantibacillus plantarum* (*L. plantarum*), which has been found to thrive in a wide range of environments, including fermented foods, several types of meat and plants, as well the mammalian gastro-intestinal tract[12]. Regarding its effects on the gastro-intestinal tract, *L. plantarum* has been shown to boost wound healing and promote anti-inflammatory processes[13].

In a series of studies, any researchers have highlighted the immune-related properties of *L. plantarum* in the gastro-intestinal tract. Our research group has shown that *L. plantarum* may participate in the alertness of the intestinal immune system, as it seems to mildly upregulate specific chemokines in subepithelial myofibroblasts[14]. In a cyclophosphamide-induced immunosuppressive animal model, Zeng *et al*[15] observed that the administration of *L. plantarum* led to the enhancement of the immune system through the restoration of inflammatory cytokines and immune markers in the spleen[15]. In another animal model of antibiotic-induced diarrhea, Liang *et al*[16] showed that the administration of *L. plantarum* ELF051 significantly improved the animals' health, by downregulating pro-inflammatory signaling pathways and cytokines, such as interleukin (IL)-1β, upregulating the anti-inflammatory ones, such as IL-10, and by enriching the

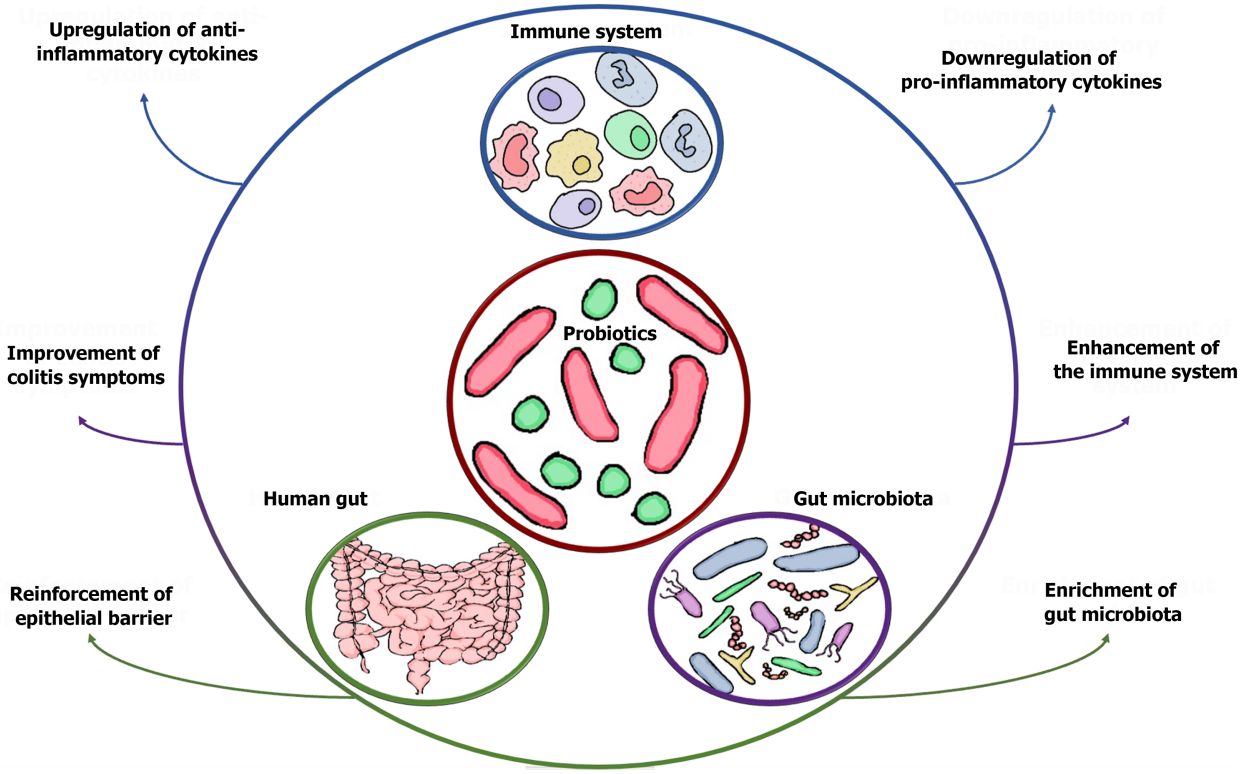

Figure 1 The beneficial effects of probiotics on the immune system, intestinal microbiota and the human gut. Probiotics promote the upregulation of anti-inflammatory cytokines, induce the downregulation of pro-inflammatory ones, improve the colitis symptoms, enhance the immune system, reinforce the epithelial barrier and favor the enrichment of the gut microbiota.

diversity of the topical gut microbiota[16]. In the same way, *L. plantarum* YRL45, a bacteriocin-producing probiotic, has been reported to favorably regulate the immune system of mice by elevating the immunoglobulins sIgA, IgA and IgG levels and by upregulating the expression of epithelial markers mucin 2, zonula occludens-1 and junctional adhesion molecule 1[17].

Similar results come from a study investigating the immunoregulatory effects of *L. plantarum* CRL681 and CRL1506 in enterotoxigenic *Escherichia coli* (*E. coli*) infection in mice; both strains found to favorably modulate the intestinal innate immune response and increase resistance to *E. coli*, ultimately leading to reduced counts of *E. coli* in the gastrointestinal tract[18]. In another study, Li *et al*[19] showed that the administration of *L. plantarum* in *E. coli*-infected mice led to a significant improvement in disease status, since it significantly stopped weight loss and restored the flattened mucosa in the jejunum, findings probably related to the significant downregulation of the proinflammatory cytokines[19]. This improvement was further enhanced when *L. plantarum* was administered along with two other probiotics, *Bifidobacterium longum* and *Pediococcus acidilactici*[19], supporting the idea that a combined rather than a single regime of probiotics is more effective.

Heat-killed fractions and proteins from *L. plantarum* 299v, now named postbiotics[20], have also proved to have anti-inflammatory properties, in the same way as live bacteria: In an lipopolysaccharides (LPS) *in vitro* model they were found to downregulate the pro-inflammatory cytokine IL-18[21], thus exerting immunomodulatory properties on the immune responses. The anti-inflammatory properties of *L. plantarum* are also highlighted by the proteomic study of Cufaro *et al* [22]: *L. plantarum* C904 was once again found able to downregulate *in vitro,* to a considerable degree pro-inflammatory cytokines, including IL-2, IL-5, IL-6, and interferon (IFN)-γ, in inflamed intestinal epithelial cells[22].

Another subspecies, the panda-derived *L. plantarum* BSG201683, when added to LPS-treated intestinal epithelial cell cultures, has been shown to strengthen their integrity, downregulate pro-inflammatory and upregulate anti-inflammatory cytokines, such as IL-10[23]. The undoubted anti-inflammatory effects of *L. plantarum* are further supported by the study of Ren *et al*[24] Mice with either acute or chronic dextran sulfate sodium (DSS)-induced colitis, when given *L. plantarum,* presented with overall improved health; the colitis symptoms improved, as did both the oxidative stress and inflammatory response[24]. The results from an LPS-induced colitis model in mice are similar; *L. plantarum* was able to ameliorate colitis, not only by counteracting its symptoms, but also by downregulating pro-inflammatory cytokines and by strengthening the epithelial barrier integrity[25].

THE GENUS LACTOBACILLUS

Lactobacillus acidophilus (*L. acidophilus*) is the most well-known probiotic species from the genus *Lactobacillus*, also having

significant anti-inflammatory properties. We have previously shown that *L. plantarum* and *L. acidophilus* are involved in the immunological alertness of the intestinal tissue, as it slightly upregulated specific chemokines in subepithelial myofibroblasts[14]. One of the metabolites of *L. acidophilus*, the indole-3-lactic acid, has been shown to act beneficially during DSS-colitis in cesarean-born mice, as its administration led to decreased intestinal inflammation and increased type-3 innate lymphoid cells (ILC3) and IL-22 Levels[26]. When bone marrow dendritic cells were co-cultured with *L. acidophilus*, it was found that the probiotic promoted both the production of IL-17 by $CD4^+$ T cells, and IL-22 by ILC3 cells [27].

In another study, *L. acidophilus* was found to improve DSS-induced colitis when in tandem with another probiotic strain, *Veillonella ratti*. By working together, these probiotics significantly restored lost body weight and colon length in mice, perhaps through short chain fatty acids (SCFA) production, while also improving overall disease activity, by downregulating pro-inflammatory cytokines and oxidative stress markers and upregulating anti-inflammatory factors [28]. The protective effects of *L. acidophilus* have also been emphasized by Aximujiang *et al*[29]: When *L. acidophilus* was given in combination with the Chinese medicine Huan Kui Le suspension, the protective effect against colitis was dramatically enhanced. The immune responses shifted towards immunoregulatory ones, and were supported by the upregulation of IL-13 and transforming growth factor-β and the downregulation of IFN-γ, the microbiota composition being once again enriched with beneficial bacteria[29].

THE GENUS LACTICASEIBACILLUS

Lacticaseibacillus rhamnosus, (formerly *Lactobacillus rhamnosus*, *L. rhamnosus*), has also been shown to exert anti-inflammatory and immunoregulating properties. Indeed, postbiotic (*i.e.* heat-killed fractions and proteins from the bacteria) of *L. rhamnosus* were also reported to downregulate the pro-inflammatory cytokine IL-18 in the LPS *in vitro* model of Magryś *et al*[21], previously described, but also to upregulate the anti-inflammatory cytokine IL-10, which *L. plantarum* failed to do[21].

Chemotherapy to fight cancer is known to induce gastrointestinal tract inflammation[30,31]. When *L. rhamnosus* was given as pretreatment, it was shown to mitigate the inflammatory responses; Nenu *et al*[32] showed that the combinational therapy of regorafenib and *L. rhamnosus* for the treatment of hepatocellular carcinoma in mice resulted in a significant reduction of inflammation and gut permeability[32], while Alsholi *et al*[33] reported that the administration of *L. rhamnosus* alleviated cisplatin-induced mucositis in an animal model[33]. Lu *et al*[34] also reported that *L. rhamnosus* GG postbiotic and antiprogrammed cell death 1 (anti-PD1) immunotherapy had better results in colorectal cancer treatment in relation to anti-PD1 immunotherapy alone. The authors observed increased populations of MHC II^+ DC cells, $CD4^+$ and $CD8^+$ T cells in the tumor sites[34], suggesting that the probiotic extracellular vesicles could boost the immune system in favor of the host, to fight the cancerous cells.

Apart from its effects on cancer-induced inflammation, *L. rhamnosus* has been also shown to have beneficial anti-inflammatory properties in DSS-colitis; Kim *et al*[35] found that the administration of *L. rhamnosus* KBL2290 in mice could ameliorate colitis by restoring body weight and colon length, reducing disease activity, and downregulating pro-inflammatory cytokines, while at the same time upregulating the anti-inflammatory IL-10[35]. The results from an LPS-induced inflammation in Caco-2 cell culture are similar; *L. rhamnosus* was found to counteract the detrimental effects of LPS on Caco-2 cells, thus enhancing their survival, reducing the inducible oxidative stress, inducing the expression of tight junction proteins and by downregulating pro-inflammatory cytokines[36]. Tomotsune *et al*[37] supported the option that the beneficial immunomodulatory effects of *L. rhamnosus* are not necessarily promoted through its adhesion to the epithelial barrier, but can also be exerted without binding to the mucus, possibly through its secreted products[37].

Finally, the beneficial effects of *L. rhamnosus* are not limited to the immune system. Chen *et al*[38] showed that this probiotic may favorably influence the epithelial barrier during sepsis, thus increasing survival time; which may occur through the increase of intestinal stem cells proliferation[38].

THE GENUS LIGILACTOBACILLUS

Ligilactobacillus [formerly known as the *Lactobacillus salivarius* (*L. salivarius*) group], are lactic acid producing, Gram-positive bacteria, commonly found in fermented foods[39]. *L. salivarius* has been characterized as a potential probiotic, due to its anti-inflammatory properties. Carbonne *et al*[40] showed that *L. salivarius* CNCM I-4866 was able to downregulate a number of pro-inflammatory markers both *in vitro* and *in vivo*, strengthen the epithelial barrier and inhibit the adherence of various intestinal pathogens to the host's epithelial cells[40].

THE GENUS LIMOSILACTOBACILLUS

The genus *Limosilactobacillus*, (formerly known as *Lactobacillus*) comprises several species able to possibly exert favorable outcomes for the host[41]. The most well-studied *Limosilactobacillus* species is *Lactobacillus fermentum* (*L. fermentum*).

Two species of the *Limosilactobacillus* genus, *L. fermentum* MN410703 and MN410702, were used to investigate whether they effectively inhibit enteric pathogens to prevent environmental enteropathy. The authors concluded that both strains have strong anti-inflammatory properties, and thus prevent chronic gut inflammation through over-expression of IL-6

and IL-10 *in vitro* and downregulation of the pro-inflammatory cytokine IL-8. Additionally, both strains were found to exert strong antagonistic properties on pathogens, adhesion to HT-29 cells, and inhibition of pathogen adherence to HT-29 cells[42].

L. fermentum has also been shown to protect against chemotherapy-induced gut permeability by regulating the expression and localization of tight-junction proteins and LPS-induced inflammation and by downregulating various pro-inflammatory cytokines. A number of authors have suggested that *L. fermentum* treatment could alleviate the adverse effects of chemotherapy in patients with colon cancer[43]. In the case of DSS-colitis, *L. fermentum* has also shown promising results as it improved the overall health of mice by restoring their lost body weight and colon length, but also by strengthening the epithelial barrier integrity through the expression of the tight-junction proteins. Additionally, it shifted the immune responses by promoting the T regulatory and suppressing the T inflammatory cells[44]. In a similar animal model of colitis, *L. fermentum* was shown to counteract inflammation by targeting the nuclear factor kappa B (NF-κB) signaling pathway, and thus downregulating several pro-inflammatory cytokines, such as tumor necrosis factor alpha (TNF)-α and IL-1β[45].

In another study which compared the possible anti-inflammatory properties of *Limosilactobacillus mucosae* (*L. mucosae*) and *Lactobacillus amylovorus* with another lactic acid bacterium, the *L. mucosae,* it was found to predominate; although both probiotics downregulated several pro-inflammatory cytokines in mice with DSS-colitis, *L. mucosae* had better effects in alleviating the colitis symptoms[46].

THE GENUS LEVILACTOBACILLUS

Levilactobacillus (formerly also known as *Lactobacillus*) is a genus of Gram-positive bacteria found mainly in fermented foods and in the composition of the intestinal microbiota[47]. One of its species, *Levilactobacillus brevis*, has been found to have promising anti-inflammatory properties, as Kim *et al*[48] showed that, when given, in inflamed HT-29 intestinal epithelial cells it resulted in the reduction of IL-8 and NF-κB levels, possibly through targeting the extracellular signal-regulated kinase and Akt signaling pathways[48].

THE GENUS BIFIDOBACTERIUM

Bifidobacterium, a genus of Gram-positive bacteria, is found both in food and in the gastrointestinal tract. Several of its species are also considered as beneficial probiotic supplements[49]. In an experimental model of excisional cutaneous trauma in rats, we have previously shown that *Bifidobacterium longum* (*B. longum*) can promote wound healing and especially angiogenesis[13]. However, its gut mucosal effect on inflammation is still under discussion. Li *et al*[19] found that the administration of *B. longum* in *E. coli*-infected mice successfully restored the lost body weight and colon length; however, it only downregulated the pro-inflammatory cytokines IL-6 and TNF-α, but not IL-1β[19]. In a similar study, where the animals were infected with *Plasmodium berghei*, *B. longum* was able to counteract the infection by diminishing parasitemia, reducing the levels of the pro-inflammatory cytokines IFN-γ and TNF-α in the serum and by enhancing an anti-inflammatory profile in the animals[50].

On the other hand, *B. longum* BAA2573 was observed to ameliorate DSS-induced colitis in mice, restoring the body weight and colon length by means of decreasing a number of disease activity markers, such as neutrophil infiltration, while, at the same time, also improving the gut microbiota diversity[51]. This action pathway leads us to believe that *B. longum* may be beneficial only in certain types of inflammation, or that it may exert its anti-inflammatory properties only when combined with other probiotics. In the study of Yue *et al*[52], when *B. longum* was given with *Bifidobacterium bifidum* to mice with LPS-induced colitis, the beneficial result was even greater than when either one was given alone. Working together these two probiotics managed to boost the immune system by elevating the IgA levels in the serum, along with increasing populations of $CD4^+/CD8^+$ T and dendritic cells. They also succeeded in strengthening the epithelial barrier by means of promoting the expression of mucus and tight junction proteins and, additionally, downregulated various pro-inflammatory cytokines[52].

Finally, bioengineered probiotics have been reported to have even greater beneficial effects on the host than simple bacteria strains[53]. One such example is *B. longum* fortified with artificial enzymes, which can lead to much reduced intestinal inflammation and enriched microbiota diversity[54].

Bifidobacterium bifidum (*B. bifidum*), on its own, has also been shown to ameliorate DSS- and trinitrobenzene sulfonic acid-induced colitis in mice. In both studies, *B. bifidum* was found to improve the overall health of the mice by restoring their body weight and colon length, strengthening the epithelial barrier integrity and the immune profile, downregulating pro-inflammatory factors and upregulating the anti-inflammatory ones[55,56]. In the case of DSS-colitis, the favorable effects of *B. bifidum* were speculated to arise through the activation of the aryl hydrocarbon receptor in the intestine[56].

Bifidobacterium breve (*B. breve*) has also been reported to possess anti-inflammatory properties. In particular, Park *et al* [57] showed that the administration of *B. breve* in two different animal models of colitis (DSS and dinitrobenzene sulfonic acid) had favorable effects, leading to the amelioration of disease severity. It increased the number of goblet cells in the intestinal epithelium and also strengthened the epithelial barrier by upregulating the mRNA of tight-junction proteins [57]. In an animal model of ileitis, the administration of a four probiotic formula comprising *Saccharomyces boulardii*, *L. rhamnosus*, *Lactobacillus acidophilus*, *B. breve* plus amylase led to a significant improvement in overall health: Disease activity was reduced, gut microbiota was enriched, and the immune system significantly boosted[58]. Nonetheless, these

beneficial effects were not observed when amylase was not given[58]. It is proposed that amylase might play a significant role in inhibiting the biofilm formation by the potentially harmful bacteria.

Bifidobacterium lactis (*B. lactis*) is known to exert promising probiotic properties. Our research group has highlighted that this probiotic may contribute to the immunological alertness of the intestinal tissue through the upregulation of specific chemokines in subepithelial myofibroblasts[14]. In the study by Lan *et al*[59], the administration of *B. lactis* in mice with DSS-induced colitis led to the amelioration of the disease (weight loss and disease activity scores were reduced), but more significantly, several pro-inflammatory cytokines were downregulated[59], strongly highlighting the anti-inflammatory properties of *B. lactis*.

Bifidobacterium pseudocatenulatum (*B. pseudocatenulatum*) is a less studies species. Wang *et al*[60] reported that the administration of *B. pseudocatenulatum* in mice with DSS-induced colitis led to an overall amelioration of the disease, the integrity of the epithelial barrier was found to be strengthened through the upregulation of tight-junction proteins and mucus production, oxidative stress was decreased by the promotion of the expression of several antioxidant enzymes and inflammation was decreased through the downregulation of pro-inflammatory cytokines and the upregulation of the anti-inflammatory IL-10[60].

Finally, *Bifidobacterium animalis* (*B. animalis*) subsp. *lactis* BLa80 has been investigated for its possible therapeutic properties in IBD. *B. animalis* subsp. *lactis* BLa80 was shown to have a favorable effect in DSS-induced colitis in mice, as it not only reduced the histological disease scores and restored the colon length, but it also downregulated pro-inflammatory cytokines and enriched the microbiota composition[61].

THE GENUS PEDIOCOCCUS

Pedioccocus is a Gram-positive, lactic acid bacterium which plays a significant role in the food fermentation process[62]. Li *et al*[19] found that the administration of *Pediococcus acidilactici* in *E. coli*-infected mice successfully restored body weight and colon length, as well as downregulating the pro-inflammatory cytokines IL-1β, IL-6 and TNF-α[19].

Another species, *Pediococcus pentosaceus* (*P. pentosaceus*) CECT8330, was investigated for its possible anti-inflammatory properties in a mouse model of DSS colitis[63,64]. The administration of *P. pentosaceus* resulted in the restoration of lost body weight and colon length, and in the reduction of disease activity and inflammation[63]. However, it is of exceptional interest to mention that *P. pentosaceus* is involved in an early switch in macrophage phenotype from the pro-inflammatory M1 to M2, in parallel with the downregulation of IL-1β levels. This finding is evidence of the acceleration of the inflammatory phase during the healing process[64].

THE GENUS AKKERMANSIA

Akkermansia is an aerotolerant anaerobe, Gram-negative bacteria, capable of growing on a viscus substrate such as mucin [65]. Although it was first isolated in 2004, it is known that it has the ability to degrade intestinal mucin glycoproteins, a process leading to the production of SCFA. Additionally, it promotes mucin turnover, thus strengthening the mucosal barrier and reducing gut permeability[66]. Liu *et al*[67] highlighted the beneficial properties of *Akkermansia muciniphila* (*A. muciniphila*) in a mouse model of antibiotic-induced diarrhea. *A. muciniphila* was found to reduce diarrhea incidents, to enhance the epithelial barrier integrity and to enrich the microbiome and metabolome profiles. Regarding the inflammation status, it resulted in the upregulation of anti-inflammatory markers, GPR109A and SLC5A8, and the downregulation of pro-inflammatory TNFα, IFN-γ, IL1β, and IL6[67]. The favorable anti-inflammatory effects of *A. muciniphila* have also been underlined by Daniel *et al*[68], being found to ameliorate the emulsifier-induced inflammation in mice through the reduction of inflammatory cell infiltration and histology scores[68].

Finally, another study underlines the favorable immunomodulatory effects of *A. muciniphila* on the gut-brain axis. A culture medium of Caco-2 intestinal epithelial cells, when pre-treated with *A. muciniphila*, exhibited an inhibitory effect on pro-inflammatory cytokine production in human microglial cells[69].

THE GENUS ROUXIELLA

The genus *Rouxiella* was first described back in 2015 by Le Flèche-Matéos *et al*[70]. One of its members, the *R. badensis* subsp. *acadiensis* (Canan SV-53), is thought to exert immunomodulatory effects, as Shahbazi *et al*[71] showed that the administration of *R. badensis* subsp. *acadiensis* in healthy mice resulted in an increase in serum IgA, a decrease in several pro-inflammatory cytokines and an increase in the anti-inflammatory subset population of cells in the small intestine[71], all probably contributing to immune system boosting. In the next experiment by the same research group on LPS-induced colitis in mice, the administration of *R. badensis* subsp. *acadiensis* led to the amelioration of disease severity through anti-inflammatory effects that mainly targeted the epigenetic mechanisms of several genes involved in the differentiation of Th17 cells[72].

THE GENUS ROSEBURIA

Roseburia are Gram-positive anaerobic bacteria. *R. intestinalis* exerts immunomodulatory effects and is a major butyrate producer in the gut[73]. Kang *et al*[74] showed that *R. intestinalis* may favor cytotoxic $CD8^+$ T cell populations during colorectal cancer, and thus boost the immune system towards fighting tumorous cells[74].

THE GENUS TETRAGENOCOCCUS

The genus *Tetragenococcus* comprises Gram-positive facultative anaerobic lactic acid bacteria[75], and among its members, *Tetragenococcus halophilus* (*T. halophilus*) has been shown to potentially protect against intestinal inflammation. In a DSS-induced colitis animal model, the administration of *T. halophilus* led to an overall amelioration of disease activity, but more significantly, it also reduced the activation of several immune-related cell populations, leading to decreased production of the pro-inflammatory cytokine IL-1β[76].

THE GENUS FAECALIBACTERIUM

The genus *Faecalibacterium* is an extremely oxygen-sensitive commensal butyrate-producer, populating the most anaerobic parts of the GI tract of mammals and is generally recognized as a biomarker of intestinal health[77]. *Faecalibacterium prausnitzii* (*F. prausnitzii*) has been found to be decreased in patients with IBD[78], and thus its (further) supplementation may lead to favorable outcomes. Indeed, in an animal model of DSS-induced colitis, the administration of Treg cells exposed to *F. prausnitzii* resulted in the amelioration of colitis, with decreased disease scores and significantly reduced inflammation[79].

THE GENUS ENTEROCOCCUS

Enterococcus is a genus of lactic acid bacteria, the species of which exert both harmful and beneficial effects[80], thus some species may be considered as possible probiotic supplements. Zheng *et al*[81] showed that *Enterococcus faecium* (*E. faecium*) could have a protective effect against the enterotoxigenic *Escherichia coli* infection, since it enhances the expression of tight-junction proteins and downregulates pro-inflammatory cytokines[81]. Benvenuti *et al*[82] suggested that the administration of *E. faecium* in obese mice resulted in reduced inflammation and improvements in the integrity of the epithelial barrier[82]. Although these results seem promising this genus has not yet received the status of "Generally Recognized As Safe" (GRAS) due to a number of potential health risks[80].

THE GENUS CLOSTRIDIUM

Clostridium is a genus of Gram-positive anaerobic bacteria and, similar to the *Enterococcus* genus, it includes both harmful and beneficial species[83]. *Clostridium butyricum* (*C. butyricum*), one of its species, exerts possible anti-inflammatory effects in experimental colitis. Indeed, extracellular vesicles (postbiotic) from this species have been shown to have anti-inflammatory properties both *in vitro* and *in vivo*, by suppressing the pro-inflammatory signaling pathways of mitogen-activated protein kinase and NF-κB through the restoration of the expression of miR-199a-3p[84]. The reduction in inflammation by means of suppression of the myeloid differentiation primary response 88 and NF-κB signaling pathways upon administration of *C. butyricum*, was also observed in an animal model of colorectal cancer[85], suggesting that *C. butyricum* could indeed be considered as a possible anti-inflammatory probiotic supplement.

THE GENUS SACCHAROMYCES

Saccharomyces is a yeast and *Saccharomyces cerevisiae* (*S. cerevisiae*) is one of the most well-known species, widely used in the food industry – brewer's yeast - but additionally serves as a very potent probiotic[86]. Regarding its role in regulating inflammation, Kil *et al*[87] showed that the administration of *S. cerevisiae* to mice with DSS-induced colitis resulted in the downregulation of neutrophil infiltration and the pro-inflammatory cytokine, TNF-α, and in upregulation of the expression of tight-junction proteins and the anti-inflammatory cytokine IL-10[87]. In transgenic rats subjected to ileocecal resection for Crohn's disease, when postoperative recurrence occurred, the administration of *S. cerevisiae* resulted in a reduction in the macroscopic and histological lesions in the anastomosis area, a decrease in *E. coli* LF82 adherence, as well as in downregulation of the pro-inflammatory IL-23 and IL-17 cytokines and upregulation of the anti-inflammatory IL-10 [88].

When four different yeasts were tested both *in vitro* and *in vivo*, *S. cerevisiae* predominate as shown to have the strongest anti-inflammatory properties. *S. cerevisiae* has also been shown to protect against experimental colitis, as the overall health of animals improved and several inflammation markers were downregulated[89].

Another yeast of the same genus is the *Saccharomyces boulardii*. We have also previously documented in relation to subepithelial myofibroblasts that it is implicated in the immunological alertness of the intestinal tissue, through a mild upregulation of specific chemokines[14].

CONCLUSION

Our assessment of the most studied probiotics led us to conclude that all genera and their species, in different ways, downregulate intestinal inflammation and enhance immune response, as follows (Table 1): Almost all genera downregulate pro-inflammatory cytokines production; less genera, mainly of *Lactobacillaceae* family upregulate the anti-inflammatory cytokines. *L. plantarum*, *L. acidophilus* and *L. rhamnosus*, *B. breve* and *B. lactis*, *R. badensis* ssp.acadiensis and *R.intestinalis* as well as *S. boulardii* enhance immune function through different pathways. Almost all genera strengthen the epithelial barrier integrity by restoring the expression of tight junction proteins and/or by promoting of mucus expression. *L. plantarum* and *L. salivarius*, *B. longum*, *B. breve*, and *B. animalis* ssp. *lactis* as well as *A. muciniphila* enhance the disturbed - due to disease - intestinal microbial diversity. *L. rhamnosus* and *B. pseudocatenulatum* promote the expression of antioxidant enzymes. *L. rhamnosus* promotes the proliferation and differentiation of intestinal stem cells; *B. breve* relieves intestinal inflammation through augmenting goblet cell regeneration; and *P. pentosaceus* shifts macrophage polarization toward the anti-inflammatory M2 phenotype. *Muciniphila* seems to exert neuroprotective effects through the 'gut-brain' axis. Almost all genera - through different mechanisms and pathways - alleviate experimental colitis symptoms.

Table 1 Probiotics on intestinal inflammation and immune responses

Probiotics	Immune system↑	Inflammatory cytokines		Epithelial barrier↑	Colitis symptoms ↓	Micro-biota diversity↑	Oxidative stress↓	Stem cells ↑	Goblet cells↑	M2 macrophages ↑	Gut-brain axis↑	Ref.
		↓Pro-	↑Anti-									
L. plantarum	+	+	+	+	+	+						[14-19, 21-25]
L. acidophilus	+	+	+		+							[14, 26-29]
L. rhamnosus	+	+	+	+	+		+	+				[21, 32-36, 38]
L. salivarius		+		+		+						[46]
L. fermentum		+	+	+	+							[42-45]
L. brevis		+										[48]
B. longum		+	+	+	+	+						[19, 50-52, 54]
B. bifidum		+	+	+	+							[55, 56]
B. breve	+			+	+	+			+			[57, 58]
B. lactis	+	+			+							[14, 59]
B. pseudo-catenulatum		+	+	+	+		+					[60]
B. animalis ssp. lactis		+			+	+						[61]
P. acidilactici		+			+							[19]
P. pentosaceus		+			+					+		[63, 64]
A. muciniphila		+	+	+		+					+	[67-69]

R. badensis ssp.acadiensis	+	+	+		+		[71, 72]
R. intestinalis	+						[74]
T. halophilus		+			+		[76]
F. prausnitzii		+			+		[79]
E. faecium		+	+	+			[81, 82]
C. butyricum		+					[84, 85]
S. cerevisiae		+	+	+	+		[87-89]
S. boulardii	+						[14]

The up↑ and down↓ arrows mean 'increase' and 'decrease', respectively.

FOOTNOTES

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REFERENCES

1 **Hill C**, Guarner F, Reid G, Gibson GR, Merenstein DJ, Pot B, Morelli L, Canani RB, Flint HJ, Salminen S, Calder PC, Sanders ME. Expert consensus document. The International Scientific Association for Probiotics and Prebiotics consensus statement on the scope and appropriate use of the term probiotic. *Nat Rev Gastroenterol Hepatol* 2014; **11**: 506-514 [PMID: 24912386 DOI: 10.1038/nrgastro.2014.66]
2 **Hotel ACP**, Cordoba A. Health and nutritional properties of probiotics in food including powder milk with live lactic acid bacteria. *Prev* 2001; **5**: 1-10
3 **Sanders ME**, Merenstein D, Merrifield CA, Hutkins R. Probiotics for human use. *Nutrit Bull* 2018; **43**: 212-225 [DOI: 10.1111/nbu.12334]
4 **Menni A**, Moysidis M, Tzikos G, Stavrou G, Tsetis JK, Shrewsbury AD, Filidou E, Kotzampassi K. Looking for the Ideal Probiotic Healing Regime. *Nutrients* 2023; **15** [PMID: 37447381 DOI: 10.3390/nu15133055]
5 **Filidou E**, Kolios G. Probiotics in Intestinal Mucosal Healing: A New Therapy or an Old Friend? *Pharmaceuticals (Basel)* 2021; **14** [PMID: 34832962 DOI: 10.3390/ph14111181]
6 **Integrative HMP (iHMP) Research Network Consortium**. The Integrative Human Microbiome Project. *Nature* 2019; **569**: 641-648 [PMID: 31142853 DOI: 10.1038/s41586-019-1238-8]
7 **Thursby E**, Juge N. Introduction to the human gut microbiota. *Biochem J* 2017; **474**: 1823-1836 [PMID: 28512250 DOI: 10.1042/BCJ20160510]
8 **Bull MJ**, Plummer NT. Part 1: The Human Gut Microbiome in Health and Disease. *Integr Med (Encinitas)* 2014; **13**: 17-22 [PMID: 26770121]
9 **Foppa C**, Rizkala T, Repici A, Hassan C, Spinelli A. Microbiota and IBD: Current knowledge and future perspectives. *Dig Liver Dis* 2023 [PMID: 38008696 DOI: 10.1016/j.dld.2023.11.015]
10 **He S**, Lin F, Hu X, Pan P. Gut Microbiome-Based Therapeutics in Critically Ill Adult Patients-A Narrative Review. *Nutrients* 2023; **15** [PMID:

38004128 DOI: 10.3390/nu15224734]
11 **Salvetti E**, Torriani S, Felis GE. The Genus Lactobacillus: A Taxonomic Update. *Probiotics Antimicrob Proteins* 2012; **4**: 217-226 [PMID: 26782181 DOI: 10.1007/s12602-012-9117-8]
12 **Filannino P**, De Angelis M, Di Cagno R, Gozzi G, Riciputi Y, Gobbetti M. How Lactobacillus plantarum shapes its transcriptome in response to contrasting habitats. *Environ Microbiol* 2018; **20**: 3700-3716 [PMID: 30094916 DOI: 10.1111/1462-2920.14372]
13 **Panagiotou D**, Filidou E, Gaitanidou M, Tarapatzi G, Spathakis M, Kandilogiannakis L, Stavrou G, Arvanitidis K, Tsetis JK, Gionga P, Shrewsbury AD, Manolopoulos VG, Kapoukranidou D, Lasithiotakis K, Kolios G, Kotzampassi K. Role of Lactiplantibacillus plantarum UBLP-40, Lactobacillus rhamnosus UBLR-58 and Bifidobacterium longum UBBL-64 in the Wound Healing Process of the Excisional Skin. *Nutrients* 2023; **15** [PMID: 37111041 DOI: 10.3390/nu15081822]
14 **Tarapatzi G**, Filidou E, Kandilogiannakis L, Spathakis M, Gaitanidou M, Arvanitidis K, Drygiannakis I, Valatas V, Kotzampassi K, Manolopoulos VG, Kolios G, Vradelis S. The Probiotic Strains Bifidobacterium lactis, Lactobacillus acidophilus, Lactiplantibacillus plantarum and Saccharomyces boulardii Regulate Wound Healing and Chemokine Responses in Human Intestinal Subepithelial Myofibroblasts. *Pharmaceuticals (Basel)* 2022; **15** [PMID: 36297405 DOI: 10.3390/ph15101293]
15 **Zeng Z**, Huang Z, Yue W, Nawaz S, Chen X, Liu J. Lactobacillus plantarum modulate gut microbiota and intestinal immunity in cyclophosphamide-treated mice model. *Biomed Pharmacother* 2023; **169**: 115812 [PMID: 37979376 DOI: 10.1016/j.biopha.2023.115812]
16 **Liang W**, Gao Y, Zhao Y, Gao L, Zhao Z, He Z, Li S. Lactiplantibacillus plantarum ELF051 Alleviates Antibiotic-Associated Diarrhea by Regulating Intestinal Inflammation and Gut Microbiota. *Probiotics Antimicrob Proteins* 2023 [PMID: 37639209 DOI: 10.1007/s12602-023-10150-x]
17 **Bu Y**, Liu Y, Zhang T, Zhang Z, Yi H. Bacteriocin-Producing Lactiplantibacillus plantarum YRL45 Enhances Intestinal Immunity and Regulates Gut Microbiota in Mice. *Nutrients* 2023; **15** [PMID: 37571374 DOI: 10.3390/nu15153437]
18 **Baillo A**, Villena J, Albarracín L, Tomokiyo M, Elean M, Fukuyama K, Quilodrán-Vega S, Fadda S, Kitazawa H. Lactiplantibacillus plantarum Strains Modulate Intestinal Innate Immune Response and Increase Resistance to Enterotoxigenic Escherichia coli Infection. *Microorganisms* 2022; **11** [PMID: 36677354 DOI: 10.3390/microorganisms11010063]
19 **Li W**, Kai L, Jiang Z, He H, Yang M, Su W, Wang Y, Jin M, Lu Z. Bifidobacterium longum, Lactobacillus plantarum and Pediococcus acidilactici Reversed ETEC-Inducing Intestinal Inflammation in Mice. *Microorganisms* 2022; **10** [PMID: 36557603 DOI: 10.3390/microorganisms10122350]
20 **Salminen S**, Collado MC, Endo A, Hill C, Lebeer S, Quigley EMM, Sanders ME, Shamir R, Swann JR, Szajewska H, Vinderola G. The International Scientific Association of Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of postbiotics. *Nat Rev Gastroenterol Hepatol* 2021; **18**: 649-667 [PMID: 33948025 DOI: 10.1038/s41575-021-00440-6]
21 **Magryś A**, Pawlik M. Postbiotic Fractions of Probiotics Lactobacillus plantarum 299v and Lactobacillus rhamnosus GG Show Immune-Modulating Effects. *Cells* 2023; **12** [PMID: 37947616 DOI: 10.3390/cells12212538]
22 **Cufaro MC**, Prete R, Di Marco F, Sabatini G, Corsetti A, Gonzalez NG, Del Boccio P, Battista N. A proteomic insight reveals the role of food-associated Lactiplantibacillus plantarum C9O4 in reverting intestinal inflammation. *iScience* 2023; **26**: 108481 [PMID: 38213792 DOI: 10.1016/j.isci.2023.108481]
23 **Zhou Y**, Duan L, Zeng Y, Song X, Pan K, Niu L, Pu Y, Li J, Khalique A, Fang J, Jing B, Zeng D, Shen B, Ni X. The panda-derived Lactiplantibacillus plantarum BSG201683 improves LPS-induced intestinal inflammation and epithelial barrier disruption in vitro. *BMC Microbiol* 2023; **23**: 249 [PMID: 37674107 DOI: 10.1186/s12866-023-02928-4]
24 **Ren R**, Zhao AQ, Chen L, Wu S, Hung WL, Wang B. Therapeutic effect of Lactobacillus plantarum JS19 on mice with dextran sulfate sodium induced acute and chronic ulcerative colitis. *J Sci Food Agric* 2023; **103**: 4143-4156 [PMID: 36573836 DOI: 10.1002/jsfa.12414]
25 **Dong J**, Ping L, Zhang K, Tang H, Liu J, Liu D, Zhao L, Evivie SE, Li B, Huo G. Immunomodulatory effects of mixed Lactobacillus plantarum on lipopolysaccharide-induced intestinal injury in mice. *Food Funct* 2022; **13**: 4914-4929 [PMID: 35395665 DOI: 10.1039/d1fo04204a]
26 **Xia Y**, Liu C, Li R, Zheng M, Feng B, Gao J, Long X, Li L, Li S, Zuo X, Li Y. Lactobacillus-derived indole-3-lactic acid ameliorates colitis in cesarean-born offspring *via* activation of aryl hydrocarbon receptor. *iScience* 2023; **26**: 108279 [PMID: 38026194 DOI: 10.1016/j.isci.2023.108279]
27 **Hrdý J**, Couturier-Maillard A, Boutillier D, Lapadatescu C, Blanc P, Procházka J, Pot B, Ryffel B, Grangette C, Chamaillard M. Oral supplementation with selected Lactobacillus acidophilus triggers IL-17-dependent innate defense response, activation of innate lymphoid cells type 3 and improves colitis. *Sci Rep* 2022; **12**: 17591 [PMID: 36266398 DOI: 10.1038/s41598-022-21643-0]
28 **Li N**, Wang H, Zhao H, Wang M, Cai J, Hao Y, Yu J, Jiang Y, Lü X, Liu B. Cooperative interactions between Veillonella ratti and Lactobacillus acidophilus ameliorate DSS-induced ulcerative colitis in mice. *Food Funct* 2023; **14**: 10475-10492 [PMID: 37934670 DOI: 10.1039/d3fo03898j]
29 **Aximujiang K**, Kaheman K, Wushouer X, Wu G, Ahemaiti A, Yunusi K. Lactobacillus acidophilus and HKL Suspension Alleviates Ulcerative Colitis in Rats by Regulating Gut Microbiota, Suppressing TLR9, and Promoting Metabolism. *Front Pharmacol* 2022; **13**: 859628 [PMID: 35600873 DOI: 10.3389/fphar.2022.859628]
30 **Hanahan D**, Weinberg RA. Hallmarks of cancer: the next generation. *Cell* 2011; **144**: 646-674 [PMID: 21376230 DOI: 10.1016/j.cell.2011.02.013]
31 **Vyas D**, Laput G, Vyas AK. Chemotherapy-enhanced inflammation may lead to the failure of therapy and metastasis. *Onco Targets Ther* 2014; **7**: 1015-1023 [PMID: 24959088 DOI: 10.2147/OTT.S60114]
32 **Nenu I**, Baldea I, Coadă CA, Crăciun RC, Moldovan R, Tudor D, Petrushev B, Toma VA, Ştefanescu H, Procopeţ B, Spârchez Z, Vodnar D, Lenghel M, Clichici S, Filip GA. Lactobacillus rhamnosus probiotic treatment modulates gut and liver inflammatory pathways in a hepatocellular carcinoma murine model. A preliminary study. *Food Chem Toxicol* 2024; **183**: 114314 [PMID: 38052407 DOI: 10.1016/j.fct.2023.114314]
33 **Alsholi DM**, Yacoub GS, Rehman AU, Ullah H, Khan AI, Deng T, Siddiqui NZ, Alioui Y, Farooqui NA, Elkharti M, Li Y, Wang L, Xin Y. Lactobacillus rhamnosus Attenuates Cisplatin-Induced Intestinal Mucositis in Mice *via* Modulating the Gut Microbiota and Improving Intestinal Inflammation. *Pathogens* 2023; **12** [PMID: 38003804 DOI: 10.3390/pathogens12111340]
34 **Lu S**, Xu J, Zhao Z, Guo Y, Zhang H, Jurutka PW, Huang D, Cao C, Cheng S. Dietary Lactobacillus rhamnosus GG extracellular vesicles enhance antiprogrammed cell death 1 (anti-PD-1) immunotherapy efficacy against colorectal cancer. *Food Funct* 2023; **14**: 10314-10328 [PMID: 37916395 DOI: 10.1039/d3fo02018e]
35 **Kim WK**, Min SG, Kwon H, Park S, Jo MJ, Ko G. Lactobacillus rhamnosus KBL2290 Ameliorates Gut Inflammation in a Mouse Model of

Dextran Sulfate Sodium-Induced Colitis. *J Microbiol* 2023; **61**: 673-682 [PMID: 37314676 DOI: 10.1007/s12275-023-00061-5]

36 **Zheng J**, Ahmad AA, Yang Y, Liang Z, Shen W, Feng M, Shen J, Lan X, Ding X. Lactobacillus rhamnosus CY12 Enhances Intestinal Barrier Function by Regulating Tight Junction Protein Expression, Oxidative Stress, and Inflammation Response in Lipopolysaccharide-Induced Caco-2 Cells. *Int J Mol Sci* 2022; **23** [PMID: 36232464 DOI: 10.3390/ijms231911162]

37 **Tomotsune K**, Raya Tonetti F, Mizuno H, Elean M, Fukuyama K, Zhou B, Ikeda-Ohtsubo W, Nishiyama K, Yamamura A, Karasawa H, Ohnuma S, Horii A, Saito T, Kitazawa H, Villena J. The Mucus Binding Factor Is Not Necessary for Lacticaseibacillus rhamnosus CRL1505 to Exert Its Immunomodulatory Activities in Local and Distal Mucosal Sites. *Int J Mol Sci* 2022; **23** [PMID: 36430834 DOI: 10.3390/ijms232214357]

38 **Chen L**, Li S, Peng C, Gui Q, Li J, Xu Z, Yang Y. Lactobacillus rhamnosus GG Promotes Recovery of the Colon Barrier in Septic Mice through Accelerating ISCs Regeneration. *Nutrients* 2023; **15** [PMID: 36771378 DOI: 10.3390/nu15030672]

39 **Zheng J**, Wittouck S, Salvetti E, Franz CMAP, Harris HMB, Mattarelli P, O'Toole PW, Pot B, Vandamme P, Walter J, Watanabe K, Wuyts S, Felis GE, Gänzle MG, Lebeer S. A taxonomic note on the genus Lactobacillus: Description of 23 novel genera, emended description of the genus Lactobacillus Beijerinck 1901, and union of Lactobacillaceae and Leuconostocaceae. *Int J Syst Evol Microbiol* 2020; **70**: 2782-2858 [PMID: 32293557 DOI: 10.1099/ijsem.0.004107]

40 **Carbonne C**, Chadi S, Kropp C, Molimard L, Chain F, Langella P, Martin R. Ligilactobacillus salivarius CNCM I-4866, a potential probiotic candidate, shows anti-inflammatory properties in vitro and in vivo. *Front Microbiol* 2023; **14**: 1270974 [PMID: 38094624 DOI: 10.3389/fmicb.2023.1270974]

41 **Ksiezarek M**, Grosso F, Ribeiro TG, Peixe L. Genomic diversity of genus Limosilactobacillus. *Microb Genom* 2022; **8** [PMID: 35838756 DOI: 10.1099/mgen.0.000847]

42 **Prakash V**, Madhavan A, Veedu AP, Babu P, Jothish A, Nair SS, Suhail A, Prabhakar M, Sain T, Rajan R, Somanathan P, Abhinand K, Nair BG, Pal S. Harnessing the probiotic properties and immunomodulatory effects of fermented food-derived Limosilactobacillus fermentum strains: implications for environmental enteropathy. *Front Nutr* 2023; **10**: 1200926 [PMID: 37342549 DOI: 10.3389/fnut.2023.1200926]

43 **De Gregorio A**, Serafino A, Krasnowska EK, Superti F, Di Fazio MR, Fuggetta MP, Hammarberg Ferri I, Fiorentini C. Protective Effect of Limosilactobacillus fermentum ME-3 against the Increase in Paracellular Permeability Induced by Chemotherapy or Inflammatory Conditions in Caco-2 Cell Models. *Int J Mol Sci* 2023; **24** [PMID: 37047193 DOI: 10.3390/ijms24076225]

44 **Kaur H**, Gupta T, Kapila S, Kapila R. Lactobacillus fermentum (MTCC-5898) based fermented whey renders prophylactic action against colitis by strengthening the gut barrier function and maintaining immune homeostasis. *Microb Pathog* 2022; **173**: 105887 [PMID: 36402346 DOI: 10.1016/j.micpath.2022.105887]

45 **Liu J**, Wang S, Yi R, Long X, Zhao X. Effect of Lactobacillus fermentum ZS40 on the NF-κB signaling pathway in an azomethane-dextran sulfate sodium-induced colon cancer mouse model. *Front Microbiol* 2022; **13**: 953905 [PMID: 36225358 DOI: 10.3389/fmicb.2022.953905]

46 **Hao Y**, Jiang L, Han D, Si D, Sun Z, Wu Z, Dai Z. Limosilactobacillus mucosae and Lactobacillus amylovorus Protect Against Experimental Colitis *via* Upregulation of Colonic 5-Hydroxytryptamine Receptor 4 and Transforming Growth Factor-β2. *J Nutr* 2023; **153**: 2512-2522 [PMID: 37356501 DOI: 10.1016/j.tjnut.2023.06.031]

47 **Liu H**, Ji HF, Zhang DY, Wang SX, Wang J, Shan DC, Wang YM. Effects of Lactobacillus brevis preparation on growth performance, fecal microflora and serum profile in weaned pigs. *Livest Sci* 2015; **178**: 251-254 [DOI: 10.1016/j.livsci.2015.06.002]

48 **Kim WJ**, Hyun JH, Lee NK, Paik HD. Protective Effects of a Novel Lactobacillus brevis Strain with Probiotic Characteristics against Staphylococcus aureus Lipoteichoic Acid-Induced Intestinal Inflammatory Response. *J Microbiol Biotechnol* 2022; **32**: 205-211 [PMID: 34750285 DOI: 10.4014/jmb.2110.10034]

49 **Alessandri G**, van Sinderen D, Ventura M. The genus bifidobacterium: From genomics to functionality of an important component of the mammalian gut microbiota running title: Bifidobacterial adaptation to and interaction with the host. *Comput Struct Biotechnol J* 2021; **19**: 1472-1487 [PMID: 33777340 DOI: 10.1016/j.csbj.2021.03.006]

50 **Fitri LE**, Sardjono TW, Winaris N, Pawestri AR, Endharti AT, Norahmawati E, Handayani D, Kurniawan SN, Azizah S, Alifia LI, Asiyah R, Ayuningtyas TR. Bifidobacterium longum Administration Diminishes Parasitemia and Inflammation During Plasmodium berghei Infection in Mice. *J Inflamm Res* 2023; **16**: 1393-1404 [PMID: 37006809 DOI: 10.2147/JIR.S400782]

51 **Lin Q**, Hao WJ, Zhou RM, Huang CL, Wang XY, Liu YS, Li XZ. Pretreatment with Bifidobacterium longum BAA2573 ameliorates dextran sulfate sodium (DSS)-induced colitis by modulating gut microbiota. *Front Microbiol* 2023; **14**: 1211259 [PMID: 37346749 DOI: 10.3389/fmicb.2023.1211259]

52 **Yue Y**, Wang Y, Xie Q, Lv X, Zhou L, Smith EE, Cao T, Zhang Y, Li B, Huo G, Ma W. Bifidobacterium bifidum E3 Combined with Bifidobacterium longum subsp. infantis E4 Improves LPS-Induced Intestinal Injury by Inhibiting the TLR4/NF-κB and MAPK Signaling Pathways In Vivo. *J Agric Food Chem* 2023; **71**: 8915-8930 [PMID: 37255290 DOI: 10.1021/acs.jafc.3c00421]

53 **Mathipa MG**, Thantsha MS. Probiotic engineering: towards development of robust probiotic strains with enhanced functional properties and for targeted control of enteric pathogens. *Gut Pathog* 2017; **9**: 28 [PMID: 28491143 DOI: 10.1186/s13099-017-0178-9]

54 **Cao F**, Jin L, Gao Y, Ding Y, Wen H, Qian Z, Zhang C, Hong L, Yang H, Zhang J, Tong Z, Wang W, Chen X, Mao Z. Artificial-enzymes-armed Bifidobacterium longum probiotics for alleviating intestinal inflammation and microbiota dysbiosis. *Nat Nanotechnol* 2023; **18**: 617-627 [PMID: 36973397 DOI: 10.1038/s41565-023-01346-x]

55 **Qu D**, Yu L, Tian F, Zhang H, Chen W, Gu Z, Zhai Q. Bifidobacterium bifidum FJSWX19M5 alleviated 2,4,6-trinitrobenzene sulfonic acid (TNBS)-induced chronic colitis by mitigating gut barrier injury and increasing regulatory T cells. *Food Funct* 2023; **14**: 181-194 [PMID: 36477762 DOI: 10.1039/d2fo02659g]

56 **Cui QY**, Tian XY, Liang X, Zhang Z, Wang R, Zhou Y, Yi HX, Gong PM, Lin K, Liu TJ, Zhang LW. Bifidobacterium bifidum relieved DSS-induced colitis in mice potentially by activating the aryl hydrocarbon receptor. *Food Funct* 2022; **13**: 5115-5123 [PMID: 35416187 DOI: 10.1039/d1fo04219j]

57 **Park IS**, Kim JH, Yu J, Shin Y, Kim K, Kim TI, Kim SW, Cheon JH. Bifidobacterium breve CBT BR3 is effective at relieving intestinal inflammation by augmenting goblet cell regeneration. *J Gastroenterol Hepatol* 2023; **38**: 1346-1354 [PMID: 37157108 DOI: 10.1111/jgh.16209]

58 **Di Martino L**, Osme A, Ghannoum M, Cominelli F. A Novel Probiotic Combination Ameliorates Crohn's Disease-Like Ileitis by Increasing Short-Chain Fatty Acid Production and Modulating Essential Adaptive Immune Pathways. *Inflamm Bowel Dis* 2023; **29**: 1105-1117 [PMID: 36715169 DOI: 10.1093/ibd/izac284]

59 **Lan H**, Liu WH, Zheng H, Feng H, Zhao W, Hung WL, Li H. Bifidobacterium lactis BL-99 protects mice with osteoporosis caused by colitis *via* gut inflammation and gut microbiota regulation. *Food Funct* 2022; **13**: 1482-1494 [PMID: 35060590 DOI: 10.1039/d1fo02218k]

60 **Wang H**, Zhang X, Kou X, Zhai Z, Hao Y. A Ropy Exopolysaccharide-Producing Strain Bifidobacterium pseudocatenulatum Bi-OTA128 Alleviates Dextran Sulfate Sodium-Induced Colitis in Mice. *Nutrients* 2023; **15** [PMID: 38068850 DOI: 10.3390/nu15234993]

61 **Dong Y**, Liao W, Tang J, Fei T, Gai Z, Han M. Bifidobacterium BLa80 mitigates colitis by altering gut microbiota and alleviating inflammation. *AMB Express* 2022; **12**: 67 [PMID: 35670877 DOI: 10.1186/s13568-022-01411-z]

62 **Todorov SD**, Dioso CM, Liong MT, Nero LA, Khosravi-Darani K, Ivanova IV. Beneficial features of pediococcus: from starter cultures and inhibitory activities to probiotic benefits. *World J Microbiol Biotechnol* 2022; **39**: 4 [PMID: 36344843 DOI: 10.1007/s11274-022-03419-w]

63 **Dong F**, Xiao F, Li X, Li Y, Wang X, Yu G, Zhang T, Wang Y. Pediococcus pentosaceus CECT 8330 protects DSS-induced colitis and regulates the intestinal microbiota and immune responses in mice. *J Transl Med* 2022; **20**: 33 [PMID: 35033121 DOI: 10.1186/s12967-022-03235-8]

64 **Hua H**, Pan C, Chen X, Jing M, Xie J, Gao Y, Huang J, Xu C, Li P. Probiotic lactic acid bacteria alleviate pediatric IBD and remodel gut microbiota by modulating macrophage polarization and suppressing epithelial apoptosis. *Front Microbiol* 2023; **14**: 1168924 [PMID: 37396394 DOI: 10.3389/fmicb.2023.1168924]

65 **González D**, Morales-Olavarria M, Vidal-Veuthey B, Cárdenas JP. Insights into early evolutionary adaptations of the Akkermansia genus to the vertebrate gut. *Front Microbiol* 2023; **14**: 1238580 [PMID: 37779688 DOI: 10.3389/fmicb.2023.1238580]

66 **Pellegrino A**, Coppola G, Santopaolo F, Gasbarrini A, Ponziani FR. Role of Akkermansia in Human Diseases: From Causation to Therapeutic Properties. *Nutrients* 2023; **15** [PMID: 37111034 DOI: 10.3390/nu15081815]

67 **Liu S**, Zhao S, Cheng Z, Ren Y, Shi X, Mu J, Ge X, Dai Y, Li L, Zhang Z. Akkermansia muciniphila Protects Against Antibiotic-Associated Diarrhea in Mice. *Probiotics Antimicrob Proteins* 2023 [PMID: 37314693 DOI: 10.1007/s12602-023-10101-6]

68 **Daniel N**, Gewirtz AT, Chassaing B. Akkermansia muciniphila counteracts the deleterious effects of dietary emulsifiers on microbiota and host metabolism. *Gut* 2023; **72**: 906-917 [PMID: 36646449 DOI: 10.1136/gutjnl-2021-326835]

69 **Zou R**, Shen G, Wu Y, Guo M, Chen J, Yang S, Zhao H, Zheng H. Akkermansia muciniphila plays a neuroprotective role in HMC3 cells through the 'gut-brain' axis. *Future Microbiol* 2023; **18**: 255-266 [PMID: 37013905 DOI: 10.2217/fmb-2022-0007]

70 **Le Flèche-Matéos A**, Levast M, Lomprez F, Arnoux Y, Andonian C, Perraud M, Vincent V, Ar Gouilh M, Thiberge JM, Vandenbogaert M, Diancourt L, Caro V, Burguière AM, Manuguerra JC. Rouxiella chamberiensis gen. nov., sp. nov., a member of the family Enterobacteriaceae isolated from parenteral nutrition bags. *Int J Syst Evol Microbiol* 2015; **65**: 1812-1818 [PMID: 25747423 DOI: 10.1099/ijs.0.000179]

71 **Shahbazi R**, Yasavoli-Sharahi H, Mallet JF, Sharifzad F, Alsadi N, Cuenin C, Cahais V, Chung FF, Herceg Z, Matar C. Novel Probiotic Bacterium Rouxiella badensis subsp. acadiensis (Canan SV-53) Modulates Gut Immunity through Epigenetic Mechanisms. *Microorganisms* 2023; **11** [PMID: 37894114 DOI: 10.3390/microorganisms11102456]

72 **Shahbazi R**, Yasavoli-Sharahi H, Alsadi N, Sharifzad F, Fang S, Cuenin C, Cahais V, Chung FF, Herceg Z, Matar C. Lentinula edodes Cultured Extract and Rouxiella badensis subsp. acadiensis (Canan SV-53) Intake Alleviates Immune Deregulation and Inflammation by Modulating Signaling Pathways and Epigenetic Mechanisms. *Int J Mol Sci* 2023; **24** [PMID: 37834058 DOI: 10.3390/ijms241914610]

73 **Nie K**, Ma K, Luo W, Shen Z, Yang Z, Xiao M, Tong T, Yang Y, Wang X. Roseburia intestinalis: A Beneficial Gut Organism From the Discoveries in Genus and Species. *Front Cell Infect Microbiol* 2021; **11**: 757718 [PMID: 34881193 DOI: 10.3389/fcimb.2021.757718]

74 **Kang X**, Liu C, Ding Y, Ni Y, Ji F, Lau HCH, Jiang L, Sung JJ, Wong SH, Yu J. Roseburia intestinalis generated butyrate boosts anti-PD-1 efficacy in colorectal cancer by activating cytotoxic CD8(+) T cells. *Gut* 2023; **72**: 2112-2122 [PMID: 37491158 DOI: 10.1136/gutjnl-2023-330291]

75 **Link T**, Vogel RF, Ehrmann MA. The diversity among the species Tetragenococcus halophilus including new isolates from a lupine seed fermentation. *BMC Microbiol* 2021; **21**: 320 [PMID: 34798831 DOI: 10.1186/s12866-021-02381-1]

76 **Islam SMS**, Ryu HM, Sohn S. Tetragenococcus halophilus Alleviates Intestinal Inflammation in Mice by Altering Gut Microbiota and Regulating Dendritic Cell Activation *via* CD83. *Cells* 2022; **11** [PMID: 35741032 DOI: 10.3390/cells11121903]

77 **Martín R**, Rios-Covian D, Huillet E, Auger S, Khazaal S, Bermúdez-Humarán LG, Sokol H, Chatel JM, Langella P. Faecalibacterium: a bacterial genus with promising human health applications. *FEMS Microbiol Rev* 2023; **47** [PMID: 37451743 DOI: 10.1093/femsre/fuad039]

78 **Gevers D**, Kugathasan S, Denson LA, Vázquez-Baeza Y, Van Treuren W, Ren B, Schwager E, Knights D, Song SJ, Yassour M, Morgan XC, Kostic AD, Luo C, González A, McDonald D, Haberman Y, Walters T, Baker S, Rosh J, Stephens M, Heyman M, Markowitz J, Baldassano R, Griffiths A, Sylvester F, Mack D, Kim S, Crandall W, Hyams J, Huttenhower C, Knight R, Xavier RJ. The treatment-naive microbiome in new-onset Crohn's disease. *Cell Host Microbe* 2014; **15**: 382-392 [PMID: 24629344 DOI: 10.1016/j.chom.2014.02.005]

79 **Touch S**, Godefroy E, Rolhion N, Danne C, Oeuvray C, Straube M, Galbert C, Brot L, Alonso Salgueiro I, Chadi S, Ledent T, Chatel JM, Langella P, Jotereau F, Altare F, Sokol H. Human CD4+CD8α+ Tregs induced by Faecalibacterium prausnitzii protect against intestinal inflammation. *JCI Insight* 2022; **7** [PMID: 35536673 DOI: 10.1172/jci.insight.154722]

80 **Hanchi H**, Mottawea W, Sebei K, Hammami R. The Genus Enterococcus: Between Probiotic Potential and Safety Concerns-An Update. *Front Microbiol* 2018; **9**: 1791 [PMID: 30123208 DOI: 10.3389/fmicb.2018.01791]

81 **Zheng H**, Pu S, Liu J, Yang F, Chen D. Enterococcus faecium inhibits NF-κB/NLRP3/Caspase-1 signaling pathway to antagonize enterotoxigenic Escherichia coli-mediated inflammatory response. *Can J Microbiol* 2023 [PMID: 38134414 DOI: 10.1139/cjm-2023-0038]

82 **Benvenuti L**, D'Antongiovanni V, Pellegrini C, Fornai M, Bernardini N, Ippolito C, Segnani C, Di Salvo C, Colucci R, Martelli A, Flori L, Calderone V, Carta G, Ghelardi E, Calvigioni M, Panattoni A, Coppolecchia R, Arini A, Antonioli L. Dietary Supplementation with the Probiotic SF68 Reinforces Intestinal Epithelial Barrier in Obese Mice by Improving Butyrate Bioavailability. *Mol Nutr Food Res* 2023; **67**: e2200442 [PMID: 37099449 DOI: 10.1002/mnfr.202200442]

83 **Guo P**, Zhang K, Ma X, He P. Clostridium species as probiotics: potentials and challenges. *J Anim Sci Biotechnol* 2020; **11**: 24 [PMID: 32099648 DOI: 10.1186/s40104-019-0402-1]

84 **Ma L**, Lyu W, Song Y, Chen K, Lv L, Yang H, Wang W, Xiao Y. Anti-Inflammatory Effect of Clostridium butyricum-Derived Extracellular Vesicles in Ulcerative Colitis: Impact on Host microRNAs Expressions and Gut Microbiome Profiles. *Mol Nutr Food Res* 2023; **67**: e2200884 [PMID: 37183784 DOI: 10.1002/mnfr.202200884]

85 **Zhou M**, Yuan W, Yang B, Pei W, Ma J, Feng Q. Clostridium butyricum inhibits the progression of colorectal cancer and alleviates intestinal inflammation *via* the myeloid differentiation factor 88 (MyD88)-nuclear factor-kappa B (NF-κB) signaling pathway. *Ann Transl Med* 2022; **10**: 478 [PMID: 35571406 DOI: 10.21037/atm-22-1670]

86 **Alsammar H**, Delneri D. An update on the diversity, ecology and biogeography of the Saccharomyces genus. *FEMS Yeast Res* 2020; **20** [PMID: 32196094 DOI: 10.1093/femsyr/foaa013]

87 **Kil BJ**, Pyung YJ, Park H, Kang JW, Yun CH, Huh CS. Probiotic potential of Saccharomyces cerevisiae GILA with alleviating intestinal

inflammation in a dextran sulfate sodium induced colitis mouse model. *Sci Rep* 2023; **13**: 6687 [PMID: 37095161 DOI: 10.1038/s41598-023-33958-7]

88 **Valibouze C**, Speca S, Dubuquoy C, Mourey F, M'Ba L, Schneider L, Titecat M, Foligné B, Genin M, Neut C, Zerbib P, Desreumaux P. Saccharomyces cerevisiae prevents postoperative recurrence of Crohn's disease modeled by ileocecal resection in HLA-B27 transgenic rats. *World J Gastroenterol* 2023; **29**: 851-866 [PMID: 36816618 DOI: 10.3748/wjg.v29.i5.851]

89 **Hu Q**, Yu L, Zhai Q, Zhao J, Tian F. Anti-Inflammatory, Barrier Maintenance, and Gut Microbiome Modulation Effects of Saccharomyces cerevisiae QHNLD8L1 on DSS-Induced Ulcerative Colitis in Mice. *Int J Mol Sci* 2023; **24** [PMID: 37047694 DOI: 10.3390/ijms24076721]

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