

We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

6,400

Open access books available

174,000

International authors and editors

190M

Downloads

Our authors are among the

154

Countries delivered to

TOP 1%

most cited scientists

12.2%

Contributors from top 500 universities



WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com



Regular Physical Activity Influences Gut Microbiota with Positive Health Effects

Mihaela Jurdana and Darja Barlič Maganja

Abstract

The gut microbiota is believed to have a major impact on human health and disease. It is involved in barrier functions and maintenance of homeostasis. It provides nutrients and metabolites, participates in a signaling network, regulates epithelial development, and influences the immune system as well as protects the intestinal mucosa from the aggression of pathogenic microorganisms. There is growing evidence that physical activity has an impact on the gut microbiota. Recent studies in animals and humans suggest that regular physical activity increases the presence of beneficial microbial species and improves host health. However, some specific differences should be noted: different forms of physical activity, frequency or intensity, aerobic or resistance training, and benefits and consequences for amateur or competitive athletes. Because the positive role of physical activity can have an impact on health and various types of diseases, the results of research studies in this area are increasingly becoming the focus of scientific interest. In addition, probiotic supplements modulate intestinal microbial flora, and the ability of probiotics to modulate perturbations in immune function after exercise highlights their potential for use in individuals exposed to high levels of physical activity.

Keywords: gut microbiota, immune system, physical exercise, health, probiotics

1. Introduction

The human gastrointestinal tract is inhabited by hundreds of thousands of microorganisms that represent highly diverse microbiota. Gut microbiota comprises a metabolically active and complex ecosystem (bacteria, archaea, viruses, and unicellular eukaryotes) that colonizes the digestive tract soon after birth [1]. It has a crucial role in establishing a dynamic association with the human organism, having crucial roles in several physiological and pathological processes [2, 3]. It protects the host from the colonization of pathogens and is linked to nutrient digestion and absorption as well as to immunological, metabolic, and motor functions [4].

In the adult gut microbiota, four major microbial phyla are known to represent over 90% of the bacterial components: *Firmicutes*, *Bacteroides*, *Proteobacteria*, and *Actinobacteria* [5]. *Firmicutes* phyla mainly include *Ruminococcus*, *Clostridium*,

Lactobacillus, *Eubacterium*, *Faecalibacterium*, and *Roseburia*, while *Bacteroides* include *Prevotella* and *Xylanibacter*. Fewer representatives are from the phyla *Actinobacteria* and *Proteobacteria* [6].

The development and maturation of gut microbiota is a dynamic process that starts in early life. Its composition may be affected by several intrinsic and extrinsic factors, like mode of delivery, mother's age, diet and metabolic status, type of feeding, family genetics, lifestyle, exercise, immunological factors, drugs like antibiotics, and availability of nutrients [7–13]. Colonization of the infant's gut was thought to begin at birth, but scientific evidence has provided indications of bacterial presence in the placenta, umbilical cord, and amniotic fluid in healthy full-term pregnancies [14–16]. These findings suggest that microbial exposure may start before delivery, allowing colonization of the fetus with maternal microbiota. Another driver affecting the microbial colonization of the infant's intestine represents the delivery mode [17]. Vagina-associated microbes such as *Lactobacillus* and *Prevotella* colonize the neonatal gut of vaginally delivered infants [18, 19], while infants which are not directly exposed to maternal microbes during C-section become colonized by environmental microorganisms from maternal skin, the hospital staff, and the hospital environment [7, 11, 19–21]. The introduction of solid food to an infant's diet changes the microbiota, and by the age of three, it resembles a relatively stable adult-like profile with a dense microbial population [12]. The composition of the gut microbiota in the adult population is relatively stable and is only transiently altered by different external factors. It is now evidenced that dietary factors, particularly the amount, type, and balance of the main dietary macronutrients (carbohydrates, proteins, and fats), and different types and intensities of exercise play an important role in shaping the gut microbiota composition [22, 23]. The preservation of healthy gut microbiota has an important role in maintaining good health, with crucial effects on mucosal barrier fortification, motility of the gut, conversion of food into required nutrients, immune system homeostasis, and protection against pathogenic microorganisms [24].

2. Microbiota metabolites in health and disease

Exercise or physical activity can greatly affect the composition of the gut microbiota. It improves several metabolic and inflammatory parameters in chronic diseases and has been used as a therapeutic strategy in chronic diseases. In this chapter, we summarize several experimental findings on the possible mechanisms by which physical activity could influence gut microbiota. We also discuss the health benefits of physical activity, probiotic consumption, and microbiota diversity. The modification in the composition and function of the gut microbiota has an impact on intestinal permeability, digestion, metabolism, and immune responses. Many diseases, from digestive to metabolic problems as well as immunological and neuropsychiatric disorders, are linked to the pro-inflammatory state caused by the alternation of gut microbiota balance [13]. The gut microbiome contributes to digestion and promotes food absorption for host energy production. Its fermentation of non-digestible dietary residues leads to metabolites such as short-chain fatty acids (SCFAs, like butyrate, acetate, and propionate), which modulate the host energy balance increasing the availability of nutrients [25]. Fermented SCFAs, secreted into the gut lumen, exceed the epithelial barrier and are released into the bloodstream. They can be used as energy sources by the intestinal microbiota and by the host cells. They could provide nearly 10% of our daily energy requirements [26]. Butyrate is used as an energy source primarily by

epithelial cells in the colon. Propionate is involved in liver gluconeogenesis [27]. It also decreases serum cholesterol levels, inhibits fatty-acid synthesis, and may be involved in weight control by stimulating satiety [28]. Acetate is metabolized in muscle tissue and can also cross the blood-brain barrier. It is used as a substrate for liver cholesterol and fatty acid synthesis [29, 30], increases colonic blood flow and oxygen uptake, and enhances ileal motility by affecting ileal contractions [31].

SCFAs can also contribute to shaping the gut environment and colon physiology, participating in different host-signaling mechanisms as well as possessing some anti-inflammatory effects [32–34]. Butyrate regulates the neutrophil function and migration, increases the expression of tight junction proteins in colon epithelia, enhances gut integrity, and activates intraepithelial lymphocytes (IELs), which express cytokines (IFN- γ and keratinocyte growth factor) to protect epithelial cells from injury [35, 36].

Besides producing SCFAs, bacterial species of the gut microbiota synthesize glycan, amino acids, and vitamins (K, B12, biotin, folate, and thiamine) and participate in the digestion of polysaccharides, increasing the amount of glucose in the liver and, therefore, increasing lipogenesis [33, 37–39].

Protective functions of microbiota are performed also through competition with pathogens for nutrients and receptors and the production of antimicrobial molecules and metabolites to avoid colonization by pathogens [40]. Through ligands from commensal bacteria (lipopolysaccharide, LPS), the gut microbiota influences the mucosal immune system development and function [41].

Gastrointestinal mucosa is a complex system acting as a physical barrier that regulates epithelial permeability. The regulation of trans-epithelial permeability allows the absorption of nutrients from the intestinal lumen through the cells lining the gut wall into the blood circulation [42]. Gut bacteria-epithelial cell interactions have been suggested as key contributors to epithelial permeability. Dysregulation of the gut microbiota and disruption of the gut mucosa enable harmful substances to pass through the barrier and can lead to the development of several chronic diseases [13, 43]. Gut dysbiosis, characterized by an imbalance in the composition and activity of gut microbial communities, has been linked to functional and inflammatory disorders [44, 45].

3. Gut microbiota composition and physical activity

Physical activity, especially moderate, has a positive effect on our body [34]. It can reduce metabolic and inflammatory diseases and influence the microbiota and health of humans and animals. Physical activity can be divided into the moderate level ($< 70\% \text{VO}_2 \text{max}$) and high-intensity level ($> 70\% \text{VO}_{2\text{max}}$). According to published studies, moderate physical activity has a positive effect on intestinal permeability, absorption and assimilation of food, and excretion of toxic metabolites [46]. In contrast, higher exercise intensity can negatively affect the digestive system and lead to the exercise-induced gastrointestinal syndrome, which affects 70% of athletes [47]. This may be the result of exercise-induced changes in the immune system of the digestive tract, leading to an increase in the inflammatory response and gastrointestinal symptoms [48].

The balance between exercise intensity, performance, and microbiota composition should be monitored for a long-time to optimize performance, health, and well-being and limit gastrointestinal syndromes.

3.1 Associations between physical activity and changes in gut microbiota in animal studies

Many animal experiments have been performed on mice and rodents, which are good models for mimicking human physiology. In animals, different forms of exercise, especially voluntary and forced, resulted in different effects on the composition of the microbiome. Many germ-free animal studies have indicated the relationship between gut microbiota and host function [49, 50]. Alteration in gut microbiota and its metabolites can affect the structure of the mucus layer and immune system after gut microbiota colonization in germ-free animals. It was demonstrated [50] that exercise training triggered changes in gut microbiota community structure in donor mice and in gut physiology in recipient mice after 5 weeks of gut microbiota transplantation and colonization. Thus, the composition of the gut microbiota of recipient mice is dependent on the physical activity of their respective donors. This suggests that physical training directly alters the host response through cytokines and the production of intestinal metabolites.

SCFAs upregulated after exercise contribute to improved energy production and reduce inflammation in the gut of physically active individuals [51]. In addition, voluntary exercise training increases host butyrate concentration and its bacterial genera, which is associated with an increase in fat-free mass in early life [52].

It is believed that an increase in butyrate levels after exercise protects against intestinal inflammation and colon cancer [53, 54]. The mechanism of these changes is not yet fully understood. However, voluntary and/or forced exercise certainly influences the composition of the gut microbiota in animals.

Maternal gut microbiota during pregnancy and lactation influences the gut microbiota of rat offspring. Physical activity during pregnancy affects maternal obesity in offspring and plasma insulin and glucose concentrations [55]. Exercises started in youth can influence the bacteria ratio. In some studies, a decrease in Firmicutes and/or an increase in Bacteroidetes was observed [56–58], while other studies showed the opposite effect [49, 59–61] or no effect [62].

Early childhood exercise can influence the composition of the gut microbiota in rats and improve the development of brain function [52]. The authors confirmed the anti-inflammatory effect of regular exercise, which protects from chronic inflammatory diseases [63].

In addition, recent studies have linked the microbiota to muscle function after antibiotic use. Depletion of the microbiota by antibiotic use resulted in decreased running performance and contractile muscle function [34, 46]. A similar effect was observed with low-carbohydrate diets, which decreased SCFA production.

3.2 Associations between physical activity and changes in gut microbiota in human studies

A positive effect of physical activity on the composition of the gut microbiota has been found in human studies and confirmed animal findings. A positive effect of moderate exercise on the gut was the shortening of stool time and contact time between pathogens and the gastrointestinal mucosa [64], so exercise prevents the risk of many inflammatory diseases and various cancers. Other possible beneficial effects of moderate exercise include reduction of LPS production, increased production of SCFAs and immunoglobulins, and increase of butyrate concentration with anticarcinogenic and anti-inflammatory properties [64].

Similar to animal studies, exercise-induced changes in microbiota diversity may reduce obesity-related complications in humans. The effect on the microbiota can be assessed by measuring diversity or functions. α -diversity represents the overall diversity of samples, while β -diversity compares how different bacterial species are distributed across different samples [42].

Based on the available studies, intense exercise, compared to moderate exercise, seems to cause more significant disturbances than moderate exercise on the human body's homeostasis [34]. High levels of inflammation (higher inflammatory interleukin-6 (IL-6)) and tumor necrosis factor-alpha (TNF- α), as well as gastrointestinal symptoms with increased intestinal permeability, were found in elite athletes [65, 66]. This may be related to diet as macronutrient intake before, during, and after exercise may influence performance and inflammatory responses in athletes [67]. Adequate carbohydrate intake after acute exercise lowers inflammatory cytokines. In addition, differences in fiber consumption impact the type and amount of SCFAs produced by microbiota [68]. Several studies have reported that fiber intake in athletes is low compared with dietary guidelines. In addition, special attention should be paid to protein supplementation in athletes. It has been demonstrated that long-term protein supplementation can have negative effects on the gut microbiota (abundance of *Bacteroidetes*) [69].

Importantly, the fitness status of participants also affects gut microbiota; individuals with good physical condition have more butyrate-producing bacterial taxa from the *Firmicutes* phylum, and 6-week intervention study in lean adults increased fecal SCFAs [34].

The World Health Organization (WHO) has published recommendations for physical activity in adults (150 minutes of moderate physical activity or at least 75 minutes of vigorous physical activity per week). The composition of the gut microbiota in women who exercised according to the recommendation of WHO was modified [70]. Similarly, in male participants with insulin resistance, both high-intensity and moderate-intensity continuous exercise resulted in an increase in *Bacteroidetes* and a decrease in inflammation [71]. A 6-month intervention with progressive exercise training leads to an increase in α -diversity as well as in the concentration of some physiologically relevant metabolites [72].

A large study conducted on 86 elite rugby athletes showed a greater gut microbiota richness/diversity compared to controls [73]. This study among elite rugby players provided evidence of the beneficial effect of exercise on gut microbiota diversity. However, the results indicated that these differences between the elite and control groups were associated with dietary extremes that could represent confounding factors.

Another study on international rugby players showed differences in the composition and functional capacity of gut microbiota as well as in microbial and human-derived metabolites [74].

In addition, a positive correlation was found between cardiorespiratory fitness (CRF), an indicator of physical fitness, and microbial diversity in 39 healthy individuals, especially in taxa that augmented the production of butyrate [75]. The authors concluded that exercise can be prescribed in patients with dysbiosis-associated diseases.

The microbiota of professional and amateur cyclists was studied by Petersen [64]. They found that the gut microbiota of professional cyclists differed from that of amateurs. In addition, a correlation between certain microorganisms in professional cyclists and high training intensities was confirmed. This study suggests that training intensity influences bacterial community structure.

Higher exercise intensity leads to changes in the gut microbiota (**Figure 1**). Exercise leads to a positive change in the bacterial composition of the gut microbiota. Higher exercise intensities require dietary intervention to prevent gastrointestinal dysfunction and inflammatory responses. Longitudinal studies monitoring exercise intensity, diet and other characteristics, and gut microbiota are still lacking. To express the intensity level of physical activity, the rate of energy expenditure expressed as metabolic equivalents (METs) is used: 1 MET is the rate of energy expenditure at rest, which for most people approximates an oxygen uptake of 3.5 milliliters per kilogram of body weight per minute (**Figure 1**).

Murtaza and coworkers [76] investigated the effects of different nutritional protocols on the fecal microbiota of elite endurance race walkers during an intense training program. This study showed that an intense training load with different dietary patterns had effects on the diversity of the gut microbiota. Specifically, it was found that a ketogenic, low-carbohydrate, and high-fat diet resulted in changes in the richness of some bacterial species [76].

Furthermore, the health benefits of physical activity in older adults have been established in several scientific studies. A relationship between physical activity and the diversity of the intestinal microbiota has been found in elderly people [77]. The abundance of *Bacteroides* significantly increased after aerobic exercise training in elderly women [78]. Results of many studies reported that gut microbiota composition does not change in some conditions, such as hypertension, obesity-associated inflammation, and gastrointestinal diseases [53, 79]. Exercise can modulate the gut microbiota diversity and could have positive effects on the pathogenesis of mentioned conditions. Since lower inflammation has been demonstrated, it is possible that exercise could decrease inflammatory markers in older adults. Exercise-induced changes in microbial composition are related to exercise duration. Recently, it has been confirmed that short-term endurance exercise in elderly men has little effect on the composition and diversity of the gut microbiota.

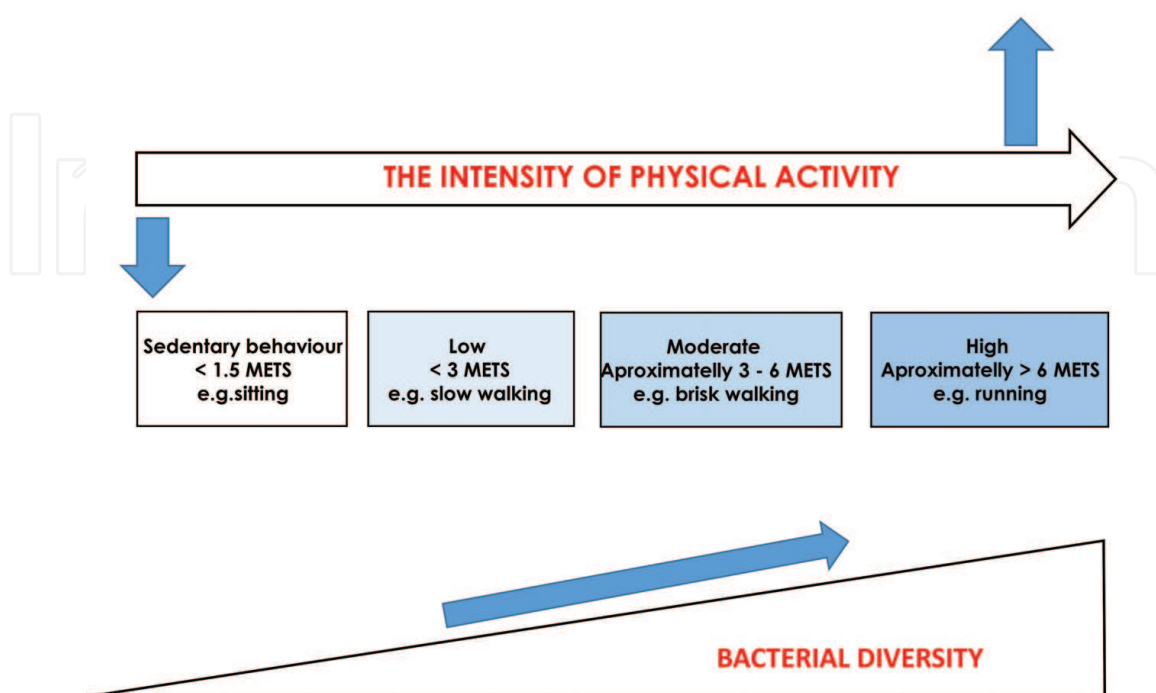


Figure 1. Exercise can increase the number of beneficial microbial species and enrich the diversity of microflora.

However, small changes in the microbiota have been associated with lower cardio-metabolic risk factors [79]. The study suggests that the gut microbiota is influenced by high-intensity exercise and diet and might play a crucial role in modulating cardiovascular disease development [80].

Overall, physical activity could be a strong modulator of gut microbiota composition. Experimental data showed that physical activity between 60 and 70% VO_{2max} affected β diversity; interestingly, exercise at 70% VO_{2max} resulted in an increase of α diversity or a decrease in *Clostridium difficile* [46].

Further studies need to clarify the effects of different types, intensities, and frequencies of physical activity on microbiota diversity and function. High intensity of physical activity decreases producers of SCFAs and increases pathogenic bacteria. This condition requires dietary supplementation [59] or a nutritional strategy [1] to maintain the structure and richness of the gut microbiota.

4. The beneficial effect of probiotics in physically active individuals

Probiotics are currently defined as live microorganisms that have a beneficial health effect on the host when consumed in adequate amounts [81, 82]. They have an impact on the intestinal ecosystem through interactions with the host cells as well as intestinal microbiota regulating gut mucosal immunity. Among others, these interactions can contribute to improving the intestinal microenvironment, strengthening the intestinal barrier, modulating mucus secretion and the secretion of immunoglobulins or cytokines, as well as activating the innate immune response.

The beneficial role of probiotics relies on their ability to modulate the host's microbiota and to improve the barrier function of the gut mucosa [83, 84]. Probiotics produce broad-spectrum inhibitory bacteriocins and metabolites such as SCFAs inducing a decrease of the pH less favorable for bacterial growth [85]. Higher SCFA concentrations also reduce the differentiation of dendritic cells, thus decreasing pro-inflammatory cytokines production [86–88].

Probiotics improve the barrier function and tight junctions (TJs) between intestinal epithelial cells at the level of signaling pathways leading to the increase of the mucus layer or to the production of defensins as well as proteins of TJs. They regulate the expression of the TJs, where cellular contacts occur and thus maintain cell morphology. As have already been reviewed, several probiotic strains, like *Lactobacillus rhamnosus* GG, *Lactobacillus casei* DN-114001, *Escherichia coli* Nissle 1917, and different strains of *Lactobacillus plantarum*, have a protective effect against pathogen infections via the regulation of TJ proteins [89].

Other important components that build a protective barrier and avoid the adhesion of harmful bacteria to the epithelial cells are the mucus layer and cells of the intestinal epithelium and underlying lamina propria [90]. Each of them consists of several cell types preventing any direct contact with bacteria in the intestinal lumen. The intestinal epithelium consists of enterocytes responsible for absorbing molecules from the intestinal lumen. Paneth cells specialized in synthesizing and secreting antimicrobial peptides (AMPs) upon contact with enteric bacteria, Goblet cells, and entero-endocrine cells [90–92]. Goblet cells produce mucus and are mainly composed of high molecular weight glycoproteins called mucins. They are of two types: secreted mucins are responsible for the formation of the mucus layer, while transmembrane mucins are likely involved in signaling pathways [93–95]. A healthy mucus layer plays an important role in preventing inflammatory and infectious diseases. Altered

expression of specific mucins was associated with gastrointestinal diseases such as Crohn's disease [96] and ulcerative colitis [97] highlighting the importance of these proteins in the intestine. Several studies confirmed that specific strains of probiotic bacteria might affect the mucus barrier by regulating mucin expression. Thus, they can influence the properties of the mucus layer and indirectly regulate the gut immune system [89]. In multiple *in vitro* and *in vivo models*, it was shown that specific probiotic bacteria stimulate the gene expression levels of mucins. Among them, *L. plantarum* 299v, *E. coli* Nissle 1917, *L. casei* GG and *Lactobacillus acidophilus* LA1, and *Lactobacillus reuteri* R2LC or 4659 as well as probiotic mixture VSL#3 were confirmed to increase the level of mucins in the gut, therefore, influencing the properties of the mucus layer and indirectly regulate the gut immune system [95, 98–103]. It has also been evidenced that *Akkermancia muciniphila* increases the number of Goblet cells and the production of antimicrobial peptides, suggesting that it communicates with host cells and consequently stimulates the production of mucus [104].

Recent findings demonstrate that probiotics modulate the intestinal immune system by activating the immune response by recognizing specific receptors of innate immunity cells (epithelial cells, dendritic cells, and T cells). These receptors are called pattern recognition receptors (PRR) and include mostly Toll-like receptors (TLRs) and nucleotide-binding oligomerization domain agents (NODs) [105]. They are recognized by MAMPs (microbe-associated molecular patterns). Their interaction with the gut epithelium stimulates the cells of the gut immune system at the lamina propria [106]. Differentiation of T helper lymphocytes and the activation of regulatory T cells stimulate the pro- or anti-inflammatory cytokines production. Probiotic bacteria, especially various *Bifidobacterium* strains, can act differently depending on the cytokine profile [107]. The effects may be systemic or local and limited to the stimulation of IgA secretion by Peyer's patch cells [108, 84].

Several studies have shown that probiotics supplementation could improve immune function in athletes [109]; reduce upper respiratory tract illness (URTI) [110], gastrointestinal symptoms [111–113], and gut permeability [114, 115]; as well as increase physical performance in elite and competitive athletes [113, 116].

Existing studies have shown an association between intestinal microbiota composition and physical activity, suggesting that modifications in the gut microbiota composition may contribute to the physical performance and exercise capacity of the host [117]. Probiotics may promote health through the improvement of the immune system and indirectly influence the performance of athletes by preventing illnesses that negatively affect healthy training [109, 118]. Recently, the International Society of Sports Nutrition (ISSN) provided a position stand on probiotics, concluding that probiotics have strain-specific effects in athletes [119]. Specific probiotic strains can improve the integrity of the gut barrier function in athletes after prolonged exercise, especially in the heat, which has been shown to increase gut permeability potentially causing systemic toxemia. Administration of selected probiotic strains has been linked to improved body composition and lean body mass, improved recovery from muscle-damaging exercise, normalizing age-related declines in testosterone levels, reductions in cortisol levels indicating improved responses to a physical or mental stressor, reduction of exercise-induced lactate, and increased neurotransmitter synthesis, cognition, and mood [reviewed in 119].

Generally, mid to long-term benefits (supplementation periods varying from 2 weeks to 3 months) of probiotics on physical performance have been studied [117]. In different studies, various probiotic strains and doses were examined, so it is

difficult to compare the obtained results. Among them, the most studied bacteria are members of *Lactobacillus* and *Bifidobacterium* genera.

Lactiplantibacillus plantarum TWK10 is among the most studied probiotic strains in terms of physical performance outcomes. A dose-dependent increase in muscle mass was observed in a preclinical animal study [120] and was further confirmed in clinical studies [121]. Endurance performance in an exhaustive treadmill exercise was improved in healthy, untrained adult males, who were supplemented daily with TWK10 for 6 weeks, compared with those who received a placebo [122]. The post-exercise blood glucose level was higher in TWK10 group compared with the control group suggesting improved energy harvest from gluconeogenic precursors during exhaustive exercise.

In male runners, supplementation with a multi-strain probiotic (*L. acidophilus*, *Lacticaseibacillus rhamnosus*, *Lacticaseibacillus casei*, *L. plantarum*, *Limosilactobacillus fermentum*, *Bifidobacterium lactis*, *B. breve*, *Bifidobacterium bifidum*, and *Streptococcus thermophilus*) for 4 weeks significantly increased the running time to fatigue [110].

Probiotic supplementation (*S. thermophilus* FP4 and *Bifidobacterium breve* BR03) was reported to likely enhance isometric average peak torque production, attenuating performance decrements and muscle tension in the days following a muscle-damaging exercise [123]. In a similar study design, *Bacillus coagulans* GBI-306086 significantly increased recovery at 24 and 72 h and decreased soreness at 72 h post-exercise [124]. Probiotic supplementation correlated with maintained performance and a small increase in creatine phosphokinase.

Probiotics, belonging to the *Veillonella* genus, isolated from a marathon runner, have recently shown promising results in mouse performance models [125]. These bacteria feed on lactic acid and produce propionate, which may increase endurance capacity.

In mice, oral administration of either *Bifidobacterium longum* subsp. *longum* OLP-01 [126] or *Ligilactobacillus salivarius* subsp. *salicinius* SA-03 [127], isolated from a female weightlifting Olympic medalist, was shown to significantly increase forelimb grip strength and endurance capacity in a swim-to-exhaustion test. Both bacterial strains significantly decreased blood lactate, ammonia, and creatine kinase levels after an acute exercise and increased hepatic and muscle glycogen stores, which indicated improved energy utilization and the attenuation of fatigue-related biomarkers in mice.

However, not all studies have shown enhancements in endurance performance following probiotic use in highly trained subjects or athletes [119]. It has been shown that the exhaustive endurance exercise was not affected in endurance-trained males after 4 weeks of *Lactobacillus fermentum* VRI-003 supplementation [128] or after *Lactobacillus helveticus* Lafti L10 in trained subjects [129]. Also, 3 months of supplementation with a probiotic formula containing bacteria of different species (*B. bifidum* W23, *B. lactis* W51, *Enterococcus faecium* W54, *L. acidophilus* W22, *Levilactobacillus brevis* W63, and *Lactococcus lactis* W58) did not have benefit in endurance performance in highly trained athletes [130]. However, after a 2-month intervention in female swimmers, probiotic yogurt with *L. acidophilus* SPP, *L. bulgaricus*, *B. bifidum*, and *S. thermophilus* improved the VO_{2max} but had no impact on the 400-m swimming time [131]. Also after a 6-week intervention in competitive, high-level, female swimmers *B. longum* 35,624 did not enhance aerobic or anaerobic swimming performance or improve power or force production measurements [132]. After a 12-week multi-strain probiotic or probiotic + glutamine supplementation, no

effects were observed on the time to complete an ultra-marathon race compared with controls [133].

Multi-strain probiotic supplementation (*L. acidophilus* CUL60 and CUL21, *B. bifidum* CUL20, and *Bifidobacterium animalis* subs p. lactis CUL34) for 28 days prior to a marathon race was associated with a limited decrease in average speed in the probiotics group compared to the control group [134]. However, there were no significant differences in finish times between the groups. *Bacillus subtilis* supplementation during training soccer and volleyball female players, in conjunction with postworkout nutrition, had no effect on physical performance [135]. However, body fat percentages were significantly lower in the probiotic group. *B. subtilis* DE111 did not improve either strength or performance in male [136] or female athletes [137] when combined with a training protocol involving resistance exercises.

Multi-strain probiotic supplementation for 12 weeks, combined with circuit training, improved muscular performance to a similar degree as circuit training alone in healthy, sedentary males [138], confirming the positive effect of resistance training on muscular outcomes, demonstrated well by other probiotic and exercise interventions among athletes [136, 137].

The well-established probiotic effects on gut health and immune system function may benefit endurance athletes, who perform high-intensity training and often encounter physiological challenges associated with GI and immune health during and after a competition. However, high-quality clinical studies, with adequate power, is necessary to uncover the impacts of probiotics on physical performance and the mechanisms of action through which probiotics affect exercise outcomes.

5. Conclusions

In recent years, the research of human gut microbiota and their interaction with their human host has extensively increased. It has been shown that the composition of the gut microbiota is influenced by several factors such as diet, age, host genetics, drugs, as well as exercise and its level of activity. Animal and human studies have indicated that gut microbiota plays an important role in the occurrence of several diseases. Mainly, it has been evidenced that its composition and function have a direct effect on host physiology and can also affect physical performance.

Exercise improves the diversity of the gut microbiota, the maintenance of normal gut physiology, and contributes to the reduction of gastrointestinal symptoms and inflammatory markers in various pathological conditions as well as altering hundreds of metabolites.

Therefore, regular physical activity should be considered as a treatment to maintain the eubiosis of the microbiota, leading to an improvement in health status. Higher CRF levels lead to greater bacterial diversity, regardless of diet. Aerobic activities appear to be able to produce significant changes in the composition of the microbiota, although the modalities and intensity of exercise may affect the microbiota differently.

The amount and frequency recommended by WHO (the minimum dose of physical activity) for adults seem to cause some changes in the composition of the microbiota. Strenuous and/or excessively prolonged exercise with inadequate carbohydrate intake may have a negative impact on the microbiota due to inflammation and gastrointestinal symptoms. Nevertheless, further studies are needed to understand how physical activity and diet independently affect the microbiota.

The use of probiotics has recently received increasing attention. Probiotics have potential health benefits, generally improving or restoring the gut microbiota, and have been shown to modulate the immune system. Recent studies have shown that probiotics reduce upper respiratory tract illness (URTI) and the onset and severity of gastrointestinal symptoms as well as gut barrier function impairment during intense exercise. By improving the immune system, they indirectly influence the performance of athletes by preventing diseases that negatively affect healthy exercise. Through SCFAs produced by probiotic bacteria, they contribute to improved energy production and reduce inflammation in the gut of physically active individuals. Selected probiotic strains have been associated with improved body composition and lean body mass, improved recovery from muscle-damaging exercise, normalization of age-related decline in testosterone levels, and reduction in cortisol levels and exercise-induced lactate. The use of probiotics is a promising approach to improve the health, well-being, and performance of athletes.

Funding

The author(s) received no specific funding for this work.

Conflict of interest

The author has no competing interest to declare that may directly or indirectly affect the content of this article.

Appendices and nomenclature

AMPs	antimicrobial peptides
CRF	cardiorespiratory fitness
IELs	intraepithelial lymphocytes
IFN- γ	interferon gamma
IL-6	interleukin-6
ISSN	international society of sports nutrition
LPS	lipopolysaccharide
MAMPs	microbe-associated molecular patterns
MET	metabolic equivalent
NODs	nucleotide-binding oligomerization domain agents
SCFAs	short-chain fatty acids
TJs	tight junctions
TLRs	toll-like receptors
TNF- α	tumor necrosis factor-alpha
URTI	upper respiratory tract illness
WHO	world health organization

IntechOpen


IntechOpen

Author details

Mihaela Jurdana* and Darja Barlič Maganja
Faculty of Health Sciences, University of Primorska, Izola, Slovenia

*Address all correspondence to: mihaela.jurdana@fvz.upr.si

IntechOpen

© 2023 The Author(s). Licensee IntechOpen. This chapter is distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/3.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. 

References

- [1] Sekirov I, Russell SL, Antunes LC, Finlay BB. Gut microbiota in health and disease. *Physiological Reviews*. 2010;**90**(3):859-904. DOI: 10.1152/physrev.00045.2009
- [2] Clemente JC, Ursell LK, Parfrey LW, Knight R. The impact of the gut microbiota on human health: An integrative view. *Cell*. 2012;**148**(6):1258-1270. DOI: 10.1016/j.cell.2012.01.035
- [3] Goulet O. Potential role of the intestinal microbiota in programming health and disease. *Nutrition Reviews*. 2015;**73**:32-40. DOI: 10.1093/nutrit/nuv039
- [4] Patel V. The gut microbiome. In: Short E, editor. *A Prescription for Healthy Living. A Guide to Lifestyle Medicine*. 2021. pp. 165-175. DOI: 10.1016/B978-0-12-821573-9.00015-1
- [5] Spor A, Koren O, Ley R. Unraveling the effects of the environment and host genotype on the gut microbiome. *Nature Reviews Microbiology*. 2011;**9**:279-290. DOI: 10.1038/nrmicro2540
- [6] Eckburg PB, Bik EM, Bernstein CN, Purdom E, Dethlefsen L, Sargent M, et al. Diversity of the human intestinal microbial flora. *Science*. 2005;**308**(5728):1635-1638. DOI: 10.1126/science.1110591
- [7] Bokulich NA, Chung J, Battaglia T, Henderson N, Jay M, Li H, et al. Antibiotics, birth mode, and diet shape microbiome maturation during early life. *Science Translational Medicine*. 2016;**8**(343):343ra82. DOI: 10.1126/scitranslmed.aad7121
- [8] Yatsunencko T, Rey FE, ManaryMJ, TrehanI, Dominguez-BelloMG, Contreras M, et al. Human gut microbiome viewed across age and geography. *Nature*. 2012;**486**(7402):222-227. DOI: 10.1038/nature11053
- [9] Kashtanova DA, Popenko AS, Tkacheva ON, Tyakht AB, Alexeev DG, Boytsov SA. Association between the gut microbiota and diet: Fetal life, early childhood, and further life. *Nutrition (Burbank, Los Angeles County, Calif.)*. 2015;**32**(6):620-627. DOI: 10.1016/j.nut.2015.12.037
- [10] Power SE, O'Toole PW, Stanton C, Ross RP, Fitzgerald GF. Intestinal microbiota, diet and health. *British Journal of Nutrition*. 2014;**111**(3):387-402. DOI: 10.1017/S0007114513002560
- [11] Rodríguez JM, Murphy K, Stanton C, Ross RP, Kobe OI, Juge N, et al. The composition of the gut microbiota throughout life, with an emphasis on early life. *Microbial Ecology in Health and Disease*. 2015;**26**(1):26050. DOI: 10.3402/mehd.v26.26050
- [12] Milani C, Duranti S, Bottacini F, Casey E, Turrone F, Mahony J, et al. The first microbial colonizers of the human gut: Composition, activities, and health implications of the infant gut microbiota. *Microbiology and Molecular Biology Reviews*. 2017;**81**(4):e00036-e00017. DOI: 10.1128/MMBR.00036-17
- [13] Gomaa EZ. Human gut microbiota/microbiome in health and diseases: A review. *Antonie Van Leeuwenhoek*. 2020;**113**(12):2019-2040. DOI: 10.1007/s10482-020-01474-7
- [14] Jiménez E, Fernández L, Marín ML, Martín R, Odriozola JM, Nueno-Palop C, et al. Isolation of commensal bacteria from umbilical cord blood of healthy

neonates born by cesarean section. *Current Microbiology*. 2005;**51**(4):270-274. DOI: 10.1007/s00284-005-0020-3

[15] DiGiulio DB, Romero R, Amogan HP, Kusanovic JP, Bik EM, Gotsch F, et al. Microbial prevalence, diversity and abundance in amniotic fluid during preterm labor: A molecular and culture-based investigation. *PLoS One*. 2008;**3**(8):e3056. DOI: 10.1371/journal.pone.0003056

[16] Aagaard K, Ma J, Antony KM, Ganu R, Petrosino J, Versalovic J. The placenta harbors a unique microbiome. *Science Translational Medicine*. 2014;**6**(237):237ra65-237ra65. DOI: 10.1126/scitranslmed.3008599

[17] Munyaka PM, Khafipour E, Ghia JE. External influence of early childhood establishment of gut microbiota and subsequent health implications. *Frontiers in Pediatrics*. 2014;**2**:109. DOI: 10.3389/fped.2014.00109

[18] Dominguez-Bello MG, Costello EK, Contreras M, Magris M, Hidalgo G, Fierer N, et al. Delivery mode shapes the acquisition and structure of the initial microbiota across multiple body habitats in newborns. *Proceedings of the National Academy of Sciences*. 2010;**107**(26):11971-11975. DOI: 10.1073/pnas.1002601107

[19] Biasucci G, Rubini M, Riboni S, Morelli L, Bessi E, Retetangos C. Mode of delivery affects the bacterial community in the newborn gut. *Early Human Development*. 2010;**86**(1):13-15. DOI: 10.1016/j.earlhumdev.2010.01.004

[20] Fouhy F, Ross RP, Fitzgerald GF, Stanton C, Cotter PD. Composition of the early intestinal microbiota: Knowledge, knowledge gaps and the use of high-throughput sequencing to address these gaps. *Gut Microbes*. 2012;**3**(3):203-220. DOI: 10.4161/gmic.20169

[21] Bäckhed F, Roswall J, Peng Y, Feng Q, Jia H, Kovatcheva-Datchary P, et al. Dynamics and stabilization of the human gut microbiome during the first year of life. *Cell Host & Microbe*. 2015;**17**(5):690-703. DOI: 10.1016/j.chom.2015.04.004

[22] Scott KP, Gratz SW, Sheridan PO, Flint HJ, Duncan SH. The influence of diet on the gut microbiota. *Pharmacological Research*. 2013;**69**(1):52-60. DOI: 10.1016/j.phrs.2012.10.020

[23] Milani C, Ticinesi A, Gerritsen J, Nouvenne A, Lugli GA, Mancabelli L, et al. Gut microbiota composition and *Clostridium difficile* infection in hospitalized elderly individuals: A metagenomic study. *Scientific Reports*. 2016;**6**(1):1-12. DOI: 10.1038/srep25945

[24] Aziz Q, Doré J, Emmanuel A, Guarner F, Quigley EMM. Gut microbiota and gastrointestinal health: Current concepts and future directions. *Neurogastroenterology & Motility*. 2013;**25**(1):4-15. DOI: 10.1111/nmo.12046

[25] Samuel BS, Shaito A, Motoike T, Rey FE, Backhed F, Manchester JK, et al. Effects of the gut microbiota on host adiposity are modulated by the short-chain fatty-acid binding G protein-coupled receptor, Gpr41. *Proceedings of the National Academy of Sciences*. 2008;**105**(43):16767-16772. DOI: 10.1073/pnas.0808567105

[26] Bergman EN. Energy contributions of volatile fatty acids from the gastrointestinal tract in various species. *Physiological Reviews*. 1990;**70**(2):567-590. DOI: 10.1152/physrev.1990.70.2.567

[27] LeBlanc JG, Chain F, Martín R, Bermúdez-Humarán LG, Courau S, Langella P. Beneficial effects on host

energy metabolism of short-chain fatty acids and vitamins produced by commensal and probiotic bacteria. *Microbial Cell Factories*. 2017;**16**(1):1-10. DOI: 10.1186/s12934-017-0691-z

[28] Hosseini E, Grootaert C, Verstraete W, Van de Wiele T. Propionate as a health-promoting microbial metabolite in the human gut. *Nutrition Reviews*. 2011;**69**(5):245-258. DOI: 10.1111/j.1753-4887.2011.00388.x

[29] Lin Y, Vonk RJ, Slooff MJ, Kuipers F, Smit MJ. Differences in propionate-induced inhibition of cholesterol and triacylglycerol synthesis between human and rat hepatocytes in primary culture. *British Journal of Nutrition*. 1995;**74**(2):197-207. DOI: 10.1079/BJN19950123

[30] Nishina PM, Freedland RA. Effects of propionate on lipid biosynthesis in isolated rat hepatocytes. *The Journal of Nutrition*. 1990;**120**(7):668-673. DOI: 10.1093/jn/120.7.668

[31] Scheppach W. Effects of short-chain fatty acids on gut morphology and function. *Gut*. 1994;**35**(Suppl. 1): S35-S38. DOI: 10.1136/gut.35.1_suppl.s35

[32] Hsu YJ, Chiu CC, Li YP, Huang WC, Te Huang Y, Huang CC, et al. Effect of intestinal microbiota on exercise performance in mice. *The Journal of Strength & Conditioning Research*. 2015;**29**(2):552-558. DOI: 10.1519/JSC.0000000000000644

[33] Wahlström A, Sayin SI, Marschall HU, Bäckhed F. Intestinal crosstalk between bile acids and microbiota and its impact on host metabolism. *Cell Metabolism*. 2016;**24**(1):41-50. DOI: 10.1016/j.cmet.2016.05.005

[34] Clauss M, Gérard P, Mosca A, Leclerc M. Interplay between exercise

and gut microbiome in the context of human health and performance. *Frontiers in Nutrition*. 2021;**8**:637010. DOI: 10.3389/fnut.2021.637010

[35] Nicholson JK, Holmes E, Kinross J, Burcelin R, Gibson G, Jia W, et al. Host-gut microbiota metabolic interactions. *Science*. 2012;**336**(6086):1262-1267. DOI: 10.1126/science.1223813

[36] Shi N, Li N, Duan X, Niu H. Interaction between the gut microbiome and mucosal immune system. *Military Medical Research*. 2017;**4**(1):1-7. DOI: 10.1186/s40779-017-0122-9

[37] Flint HJ, Scott KP, Duncan SH, Louis P, Forano E. Microbial degradation of complex carbohydrates in the gut. *Gut Microbes*. 2012;**3**(4):289-306. DOI: 10.4161/gmic.19897

[38] Brahe LK, Astrup A, Larsen LH. Can we prevent obesity-related metabolic diseases by dietary modulation of the gut microbiota? *Advances in Nutrition*. 2016;**7**(1):90-101. DOI: 10.3945/an.115.010587

[39] Molinero N, Ruiz L, Sánchez B, Margolles A, Delgado S. Intestinal bacteria interplay with bile and cholesterol metabolism: Implications on host physiology. *Frontiers in Physiology*. 2019;**10**:185. DOI: 10.3389/fphys.2019.00185

[40] Akira S, Hemmi H. Recognition of pathogen-associated molecular patterns by TLR family. *Immunology Letters*. 2003;**85**(2):85-95. DOI: 10.1016/S0165-2478(02)00228-6

[41] Rakoff-Nahoum S, Paglino J, Eslami-Varzaneh F, Edberg S, Medzhitov R. Recognition of commensal microflora by toll-like receptors is required for intestinal homeostasis. *Cell*. 2004;**118**(2):229-241. DOI: 10.1016/j.cell.2004.07.002

- [42] Bjarnason I, Macpherson A, Hollander D. Intestinal permeability: An overview. *Gastroenterology*. 1995;**108**(5):1566-1581. DOI: 10.1016/0016-5085(95)90708-4
- [43] Vancamelbeke M, Vermeire S. The intestinal barrier: A fundamental role in health and disease. *Expert Review of Gastroenterology & Hepatology*. 2017;**11**(9):821-834. DOI: 10.1080/17474124.2017.1343143
- [44] Natividad JM, Verdu EF. Modulation of intestinal barrier by intestinal microbiota: Pathological and therapeutic implications. *Pharmacological Research*. 2013;**69**(1):42-51. DOI: 10.1016/j.phrs.2012.10.007
- [45] Allam-Ndoul B, Castonguay-Paradis S, Veilleux A. Gut microbiota and intestinal trans-epithelial permeability. *International Journal of Molecular Sciences*. 2020;**21**(17):6402. DOI: 10.3390/ijms21176402
- [46] Dziewiecka H, Buttar HS, Kasperska A, Ostapiuk-Karolczuk J, Domagalska M, Cichoń J, et al. Physical activity induced alterations of gut microbiota in humans: A systematic review. *BMC Sports Science, Medicine & Rehabilitation*. 2022;**14**(1):122. DOI: 10.1186/s13102-022-00513-2
- [47] Ribeiro FM, Petriz B, Marques G, Kamilla LH, Franco OL. Is there an exercise-intensity threshold capable of avoiding the leaky gut? *Frontiers in Nutrition*. 2021;**8**:627-289. DOI: 10.3389/fnut.2021.627289
- [48] Camilleri M. Leaky gut: Mechanisms, measurement and clinical implications in humans. *Gut*. 2019;**68**(8):1516-1526. DOI: 10.1136/gutjnl-2019-318427
- [49] Choi J, Eum SY, Rampersaud E, Daunert S, Abreu MT, Toborek M. Exercise attenuates PCB-induced changes in the mouse gut microbiome. *Environmental Health Perspectives*. 2013;**121**(6):725-730. DOI: 10.1289/ehp.1306534
- [50] Allen JM, Mailing LJ, Cohrs J, Salmonson C, Fryer JD, Nehra V, et al. Exercise training-induced modification of the gut microbiota persists after microbiota colonization and attenuates the response to chemically-induced colitis in gnotobiotic mice. *Gut Microbes*. 2018;**9**(2):115-130. DOI: 10.1080/19490976.2017.1372077
- [51] Turnbaugh PJ, Ley RE, Mahowald MA, Magrini V, Mardis ER, Gordon JI. An obesity-associated gut microbiome with increased capacity for energy harvest. *Nature*. 2006;**444**(7122):1027-1031. DOI: 10.1038/nature05414
- [52] Mika A, Van Treuren W, González A, Herrera JJ, Knight R, Fleshner M. Exercise is more effective at altering gut microbial composition and producing stable changes in lean mass in juvenile versus adult male F344 rats. *PLoS One*. 2015;**10**(5):e0125889. DOI: 10.1371/journal.pone.0125889
- [53] Monda V, Villano I, Messina A, Valenzano A, Esposito T, Moscatelli F, et al. Exercise modifies the gut microbiota with positive health effects. *Oxidative Medicine and Cellular Longevity*. 2017;**2017**:3831972. DOI: 10.1155/2017/3831972
- [54] Matsumoto M, Inoue R, Tsukahara T, Ushida K, Chij H, Matsubara N, et al. Voluntary running exercise alters microbiota composition and increases n-butyrate concentration in the rat cecum. *Bioscience, Biotechnology and Biochemistry*. 2008;**72**(2):572-576. DOI: 10.1271/bbb.70474

- [55] Bhagavata Srinivasan SP, Raipuria M, Bahari H, Kaakoush NO, Morris MJ. Impacts of diet and exercise on maternal gut microbiota are transferred to offspring. *Front Endocrinol (Lausanne)*. 2018;**9**:716. DOI: 10.3389/fendo.2018.00716
- [56] Queipo-Ortuño MI, Seoane LM, Murri M, Pardo M, Gomez-Zumaquero JM, Cardona F, et al. Gut microbiota composition in male rat models under different nutritional status and physical activity and its association with serum leptin and ghrelin levels. *PLoS One*. 2013;**8**(5):e65465. DOI: 10.1371/journal.pone.0065465
- [57] Denou E, Marcinko K, Surette MG, Steinberg GR, Schertzer JD. High-intensity exercise training increases the diversity and metabolic capacity of the mouse distal gut microbiota during diet-induced obesity. *American Journal of Physiology-Endocrinology and Metabolism*. 2016;**310**(11):E982-E993. DOI: 10.1152/ajpendo.00537.2015
- [58] Brandt N, Kotowska D, Kristensen CM, Olesen J, Lützhøft DO, Halling JF, et al. The impact of exercise training and resveratrol supplementation on gut microbiota composition in high-fat diet fed mice. *Physiological Reports*. 2018;**6**(20):e13881. DOI: 10.14814/phy2.13881
- [59] Kang SS, Jeraldo PR, Kurti A, Miller MEB, Cook MD, Whitlock K, et al. Diet and exercise orthogonally alter the gut microbiome and reveal independent associations with anxiety and cognition. *Molecular Neurodegeneration*. 2014;**9**:1. DOI: 10.1186/1750-1326-9-36
- [60] Lambert JE, Myslicki JP, Bomhof MR, Belke DD, Shearer J, Reimer RA. Exercise training modifies gut microbiota in normal and diabetic mice. *Applied Physiology Nutrition and Metabolism*. 2015;**40**:749-752. DOI: 10.1139/apnm-2014-0452
- [61] Feng X, Uchida Y, Koch L, Britton S, Hu J, Lutrin D, et al. Exercise prevents enhanced postoperative neuroinflammation and cognitive decline and rectifies the gut microbiome in a rat model of metabolic syndrome. *Frontiers in Immunology*. 2017;**8**:1768. DOI: 10.3389/fimmu.2017.01768
- [62] Okamoto T, Morino K, Ugi S, Nakagawa F, Lemecha M, Ida S, et al. Microbiome potentiates endurance exercise through intestinal acetate production. *The American Journal of Physiology-Endocrinology and Metabolism*. 2019;**316**:E956-E966. DOI: 10.1152/ajpendo.00510.2018
- [63] Cook MD, Allen JM, Pence BD, Wallig MA, Gaskins HR, White BA, et al. Exercise and gut immune function: Evidence of alterations in colon immune cell homeostasis and microbiome characteristics with exercise training. *Immunology and Cell Biology*. 2016;**94**(2):158-163. DOI: 10.1038/icb.2015.108
- [64] Petersen LM, Bautista EJ, Nguyen H, Hanson BM, Chen L, Lek SH, et al. Community characteristics of the gut microbiomes of competitive cyclists. *Microbiome*. 2017;**5**(1):98. DOI: 10.1186/s40168-017-0320-4
- [65] Castell LM, Poortmans JR, Leclercq R, Brasseur M, Duchateau J, Newsholme EA. Some aspects of the acute phase response after a marathon race, and the effects of glutamine supplementation. *The European Journal of Applied Physiology*. 1996;**75**:47-53. DOI: 10.1007/s004210050125
- [66] Suzuki K, Yamada M, Kurakake S, Okamura N, Yamaya K, Liu Q, et al. Circulating cytokines and hormones with immunosuppressive but

neutrophil-priming potentials rise after endurance exercise in humans. *The European Journal of Applied Physiology*. 2000;**81**:281-287. DOI: 10.1007/s004210050044

[67] Jurdana M, Jenko Pražnikar Z, Jakus T. Macronutrient intake and energy availability in young male elite cyclists: The importance of adequate CHO intake: CHO intake in young elite cyclists. *Progress in Nutrition [Internet]*. 2022;**24**(3):e2022096. Available from: <https://mattioli1885journals.com/index.php/progressinnutrition/article/view/12439>

[68] Besten G den, Eunen K van, Groen AK, Venema K, Reijngoud D-J, Bakker BM. The role of short-chain fatty acids in the interplay between diet, gut microbiota, and host energy metabolism. *The Journal of Lipid Research*. 2013; **54**: 2325-2340. DOI: 10.1194/jlr.R036012

[69] Moreno-Pérez D, Bressa C, Bailén M, Hamed-Bousdar S, Naclerio F, Carmona M, et al. Effect of a protein supplement on the gut microbiota of endurance athletes: A randomized, controlled, double-blind pilot study. *Nutrients*. 2018;**10**(3):337. DOI: 10.33710.3390/nu10030337

[70] Bressa C, Bailén-Andrino M, Pérez-Santiago J, González-Soltero R, Pérez M, Montalvo-Lominchar MG, et al. Differences in gut microbiota profile between women with active lifestyle and sedentary women. *PLoS One*. 2017;**12**:e0171352. DOI: 10.1371/journal.pone.0171352

[71] Motiani KK, Collado MC, Eskelinen JJ, Virtanen KA, Löyttyniemi E, Salminen S, et al. Exercise training modulates gut microbiota profile and improves endotoxemia. *Medicine and Science in Sports and*

Exercise. 2020;**52**:94-104. DOI: 10.1249/MSS.0000000000002112

[72] Barton W, Cronin O, Garcia-Perez I, Whiston R, Holmes E, Woods T, et al. The effects of sustained fitness improvement on the gut microbiome: A longitudinal, repeated measures case-study approach. *Translational Sports Medicine*. 2021;**4**:174-192. DOI: 10.1002/tsm2.215

[73] Clarke SF, Murphy EF, O'Sullivan O, Lucey AJ, Humphrey M, Hogan A, et al. Exercise and associated dietary extremes impact on gut microbial diversity. *Gut*. 2014;**63**(12):1913-1920. DOI: 10.1136/gutjnl-2013-306541

[74] O'Donovan CM, Madigan SM, Garcia-Perez I, Rankin A, O'Sullivan O, Cotter PD. Distinct microbiome composition and metabolome exists across subgroups of elite Irish athletes. *The Journal of Science and Medicine in Sport*. 2020;**23**:63-68. DOI: 10.1016/j.jsams.2019.08.290

[75] Estaki M, Pither J, Baumeister P, et al. Cardiorespiratory fitness as a predictor of intestinal microbial diversity and distinct metagenomic functions. *Microbiome*. 2016;**4**(1):42. Published 2016 Aug 8. DOI: 10.1186/s40168-016-0189-7

[76] Murtaza N, Burke LM, Vlahovich N, Little JP, Gill SK, Ghosh S, et al. The effects of dietary pattern during intensified training on stool microbiota of elite race walkers. *Nutrients*. 2019;**11**(2):261. DOI: 10.3390/nu11020261

[77] Jackson MA, Jeffery IB, Beaumont M, Bell JT, Clark AG, Ley RE, et al. Signatures of early frailty in the gut microbiota. *Genome Medicine*. 2016;**8**(1):8. DOI: 10.1186/s13073-016-0262-7

- [78] Morita E, Yokoyama H, Imai D, Takeda R, Ota A, Kawai E, et al. Aerobic exercise training with brisk walking increases intestinal bacteroides in healthy elderly women. *Nutrients*. 2019;**11**:868. DOI: 10.3390/nu11040868
- [79] Taniguchi H, Tanisawa K, Sun X, Kubo T, Hoshino Y, Hosokawa M, et al. Effects of short-term endurance exercise on gut microbiota in elderly men. *Physiological Reports*. 2018;**6**(23):e13935. DOI: 10.14814/phy2.13935
- [80] Juneau M, Hayami D, Gayda M, Lacroix S, Nigam A. Provocative issues in heart disease prevention. *The Canadian Journal of Cardiology*. 2014;**30**(12Suppl):S401-S409. DOI: 10.1016/j.cjca.2014.09.014
- [81] Anonyme. Report of a joint FAO/WHO expert consultation. Guidelines for the evaluation of probiotics in food. London, Canada. April 2002. Available from: <http://www.fda.gov/ohrms/dockets/dockets/95s0316/95s-0316-rpt0282-tab-03-ref-19-joint-faowho-vol219.pdf>
- [82] Pawar R, Dhawal P, Nabar B, Barve S, Zambare V. Mechanism and applications of probiotics in healthcare industry. In: *Biotechnology in Healthcare: Applications and Initiative*, Volume 2, D. Barh (ed), Elsevier: London, UK. 2022; pp. 225-245. DOI: 10.1016/B978-0-323-90042-3.00002-5. ISBN: 978-0-323-90042-3
- [83] Hill C, Guarner F, Reid G, Gibson GR, Merenstein DJ, Pot B, et al. The international scientific association for probiotics and prebiotics consensus statement on the scope and appropriate use of the term probiotic. *Nature Reviews Gastroenterology & Hepatology*. 2014;**11**:506-514. DOI: 10.1038/nrgastro.2014.66
- [84] Kim SK, Guevarra RB, Kim YT, Kwon J, Kim H, Cho JH, et al. Role of probiotics in human gut microbiome-associated diseases. *Journal of Microbiology and Biotechnology*. 2019;**29**:1335-1340. DOI: 10.4014/jmb.1906.06064
- [85] Butel M-J. Probiotics, gut microbiota and health. *Médecine et Maladies Infectieuses*. 2014;**44**(1):1-8. DOI: 10.1016/j.medmal.2013.10.002
- [86] Liu L, Li L, Min J, Wang J, Wu H, Zeng Y, et al. Butyrate interferes with the differentiation and function of human monocyte-derived dendritic cells. *Cellular Immunology*. 2012;**277**(1-2):66-73. DOI: 10.1016/j.cellimm.2012.05.011
- [87] Corrêa-Oliveira R, Fachi JL, Vieira A, Sato FT, Vinolo MAR. Regulation of immune cell function by short-chain fatty acids. *Clinical & Translational Immunology*. 2016;**5**:e73. DOI: 10.1038/cti.2016.17
- [88] Martin-Gallausiaux C, Marinelli L, Blottière HM, Larraufie P, Lapaque N. SCFA: Mechanisms and functional importance in the gut. *Proceedings of the Nutrition Society*. 2021;**80**(1):37-49. DOI: 10.1017/S0029665120006916
- [89] La Fata G, Weber P, Mohajeri MH. Probiotics and the gut immune system: Indirect regulation. *Probiotics and Antimicrobial Proteins*. 2018;**10**:11-21. DOI: 10.1007/s12602-017-9322-6
- [90] De Santis S, Cavalcanti E, Mastronardi M, Jirillo E, Chieppa M. Nutritional keys for intestinal barrier modulation. *Frontiers in Immunology*. 2015;**6**:612. DOI: 10.3389/fimmu.2015.00612
- [91] Lievin-Le Moal V, Servin AL. Anti-infective activities of lactobacillus strains in the human intestinal microbiota: From probiotics to gastrointestinal

anti-infectious biotherapeutic agents. *Clinical Microbiology Reviews*. 2014;**27**:167-199. DOI: 10.1128/CMR.00080-13

[92] Vaishnava S, Behrendt CL, Ismail AS, Eckmann L, Hooper LV. Paneth cells directly sense gut commensals and maintain homeostasis at the intestinal host-microbial interface. *PNAS*. 2008;**105**:20858-20863. DOI: 10.1073/pnas.0808723105

[93] Corfield AP, Myerscough N, Longman R, Sylvester P, Arul S, Pignatelli M. Mucins and mucosal protection in the gastrointestinal tract: New prospects for mucins in the pathology of gastrointestinal disease. *Gut*. 2000;**47**:589-594. DOI: 10.1136/gut.47.4.589

[94] Cornick S, Tawiah A, Chadee K. Roles and regulation of the mucus barrier in the gut. *Tissue Barriers*. 2015;**3**:e982426. DOI: 10.4161/21688370.2014.982426

[95] Mack DR, Michail S, Wei S, McDougall L, Hollingsworth MA. Probiotics inhibit enteropathogenic *E. Coli* adherence in vitro by inducing intestinal mucin gene expression. *American Journal of Physiology*. 1999;**276**:G941-G950. DOI: 10.1152/ajpgi.1999.276.4.G941

[96] Buisine MP, Desreumaux P, Leteurtre E, Copin MC, Colombel JF, Porchet N, et al. Mucin gene expression in intestinal epithelial cells in Crohn's disease. *Gut*. 2001;**49**:544-551. DOI: 10.1136/gut.49.4.544

[97] Rhodes JM. Colonic mucus and ulcerative colitis. *Gut*. 1997;**40**:80-808. DOI: 10.1136/gut.40.6.807

[98] Bernet MF, Brassart D, Neeser JR, Servin AL. *Lactobacillus acidophilus* LA 1 binds to cultured human intestinal cell

lines and inhibits cell attachment and cell invasion by enterovirulent bacteria. *Gut*. 1994;**35**:483-489. DOI: 10.1136/gut.40.6.807

[99] Hafez MM. Upregulation of intestinal mucin expression by the probiotic bacterium *E. coli* Nissle 1917. *Probiotics and Antimicrobial Proteins*. 2012;**4**:67-77. DOI: 10.1007/s12602-012-9092-0

[100] Hardy H, Harris J, Lyon E, Beal J, Foey AD. Probiotics, prebiotics and immunomodulation of gut mucosal defences: Homeostasis and immunopathology. *Nutrients*. 2013;**5**:1869-1912. DOI: 10.3390/nu5061869

[101] Mattar AF, Teitelbaum DH, Drongowski RA, Yongyi F, Harmon CM, Coran AG. Probiotics up-regulate MUC-2 mucin gene expression in a Caco-2 cell-culture model. *Pediatric Surgery International*. 2002;**18**:586-590. DOI: 10.1007/s00383-002-0855-7

[102] Caballero-Franco C, Keller K, De Simone C, Chadee K. The VSL#3 probiotic formula induces mucin gene expression and secretion in colonic epithelial cells. *American Journal of Physiology. Gastrointestinal and Liver Physiology*. 2007;**292**:G315-G322. DOI: 10.1152/ajpgi.00265.2006

[103] Ahl D, Liu H, Schreiber O, Ross S, Phillipson M, Holm L. *Lactobacillus reuteri* increases mucus thickness and ameliorates dextran sulphate sodium-induced colitis in mice. *Acta Physiologica*. 2016;**217**:300-310. DOI: 10.1111/apha.12695

[104] van der Lugt B, van Beek AA, Aalvink S, et al. *Akkermansia muciniphila* ameliorates the age-related decline in colonic mucus thickness and attenuates immune activation in

accelerated aging Ercc1- Δ 7 mice. *Immunity and Ageing*. 2019;**16**:6. DOI: 10.1186/s12979-019-0145-z

[105] Wu H, Chen X, Zhang S, Li J. Gut microbiota, the potential biological medicine for prevention, intervention and drug sensitization to fight diseases. *Nutrients*. 2022;**14**:4220. DOI: 10.3390/nu14204220

[106] Round JL, Mazmanian SK. The gut microbiome shapes intestinal immune responses during health and disease. *Nature Reviews Immunology*. 2009;**9**(5):313-323. DOI: 10.1038/nri2515

[107] Menard O, Butel MJ, Gaboriau-Routhiau V, Waligora-Dupriet AJ. Gnotobiotic mouse immune response induced by *Bifidobacterium* sp. strains isolated from infants. *Applied and Environmental Microbiology*. 2008;**74**:660-666. DOI: 10.1128/AEM.01261-07

[108] Shang J, Wan F, Zhao L, Meng X, Li B. Potential immunomodulatory activity of a selected strain *Bifidobacterium bifidum* H3-R2 as evidenced in vitro and in immunosuppressed mice. *Frontiers in Microbiology*. 2020;**11**:2089. DOI: 10.3389/fmicb.2020.02089

[109] Leite GSF, Resende AS, West NP, Lancha AH. Probiotics and sports: A new magic bullet? *Nutrients*. 2019;**60**:152-160. DOI: 10.1016/j.nut.2018.09.023

[110] Shing CM, Peake JM, Lim CL, Briskey D, Walsh NP, Fortes MB, et al. Effects of probiotics supplementation on gastrointestinal permeability, inflammation and exercise performance in the heat. *European Journal of Applied Physiology*. 2014;**114**:93-103. DOI: 10.1007/s00421-013-2748-y

[111] Łagowska K, Bajerska J, Kamiński S, Del Bo' C. Effects of probiotics supplementation on gastrointestinal symptoms in athletes: A systematic review of randomized controlled trials. *Nutrients*. 2022;**14**:2645. DOI: 10.3390/nu14132645

[112] Quero CD, Manonelles P, Fernández M, Abellán-Aynés O, López-Plaza D, Andreu-Caravaca L, et al. Differential health effects on inflammatory, immunological and stress parameters in professional soccer players and sedentary individuals after consuming a synbiotic. A triple-blinded, randomised, placebo-controlled pilot study. *Nutrients*. 2021;**13**:1321. DOI: 10.3390/nu13041321

[113] Maughan RJ, Burke LM, Dvorak J, Larson-Meyer DE, Peeling P, Phillips SM, et al. IOC consensus statement: Dietary supplements and the high-performance athlete. *International Journal of Sport Nutrition and Exercise Metabolism*. 2018;**28**:104-125. DOI: 10.1123/ijsnem.2018-0020

[114] Kekkonen RA, Vasankari TJ, Vuorimaa T, Haahtela T, Julkunen I, Korpela R. The effect of probiotics on respiratory infections and gastrointestinal symptoms during training in marathon runners. *International Journal of Sport Nutrition and Exercise Metabolism*. 2007;**17**:352-363. DOI: 10.1123/ijsnem.17.4.352

[115] Schreiber C, Tamir S, Golan R, Weinstein A, Weinstein Y. The effect of probiotic supplementation on performance, inflammatory markers and gastrointestinal symptoms in elite road cyclists. *Journal of International Society of Sports Nutrition*. 2021;**18**:36. DOI: 10.1186/s12970-021-00432-6

[116] Roberts J, Suckling C, Peedle G, Murphy J, Dawkins T, Roberts M. An exploratory investigation of endotoxin

- levels in novice long distance triathletes, and the effects of a multi-strain probiotic/prebiotic, antioxidant intervention. *Nutrients*. 2016;**8**:733. DOI: 10.3390/nu8110733
- [117] Marttinen M, Ala-Jaakkola R, Laitila A, Lehtinen MJ. Gut microbiota, probiotics and physical performance in athletes and physically active individuals. *Nutrients*. 2020;**12**(10):2936. DOI: 10.3390/nu12102936
- [118] Colbey C, Cox AJ, Pyne DB, Zhang P, Cripps AW, West NP. Upper respiratory symptoms, gut health and mucosal immunity in athletes. *Sports Medicine*. 2018;**48**(Suppl. 1):65-77. DOI: 10.1007/s40279-017-0846-4
- [119] Jäger R, Mohr AE, Carpenter KC, Kerksick CM, Purpura M, Moussa A, et al. International society of sports nutrition position stand: Probiotics. *Journal of International Society of Sports Nutrition*. 2019;**16**(1):62. DOI: 10.1186/s12970-019-0329-0
- [120] Chen YM, Wei L, Chiu YS, Hsu YJ, Tsai TY, Wang MF, et al. *Lactobacillus plantarum* TWK10 supplementation improves exercise performance and increases muscle mass in mice. *Nutrients*. 2016;**8**(4):205. DOI: 10.3390/nu8040205
- [121] Huang WC, Lee MC, Lee CC, Ng KS, Hsu YJ, Tsai TY, et al. Effect of *Lactobacillus plantarum* TWK10 on exercise physiological adaptation, performance, and body composition in healthy humans. *Nutrients*. 2019;**11**:2836. DOI: 10.3390/nu11112836
- [122] Huang WC, Hsu YJ, Li H, Kan NW, Chen YM, Lin JS, et al. Effect of *Lactobacillus plantarum* TWK10 on improving endurance performance in humans. *Chinese Journal of Physiology*. 2018;**61**:163-170. DOI: 10.4077/CJP.2018.BAH587
- [123] O'Brien KV, Stewart LK, Forney LA, Aryana KJ, Prinyawiwatkul W, Boeneke CA. The effects of postexercise consumption of a kefir beverage on performance and recovery during intensive endurance training. *Journal of Dairy Science*. 2015;**98**:7446-7449. DOI: 10.3168/jds.2015-9392
- [124] Salehzadeh K. The effects of probiotic yogurt drink on lipid profile, CRP and record changes in aerobic athletes. *International Journal of Life Sciences*. 2015;**9**:32-37. DOI: 10.3126/ijls.v9i4.12672
- [125] Peake JM, Neubauer O, Della Gatta PA, Nosaka K. Muscle damage and inflammation during recovery from exercise. *Journal of Applied Physiology*. 2017;**122**:559-570. DOI: 10.1152/jappphysiol.00971.2016
- [126] Lee MC, Hsu YJ, Chuang HL, Hsieh PS, Ho HH, Chen WL, et al. *In vivo* ergogenic properties of the *Bifidobacterium longum* OLP-01 isolated from a weightlifting gold medalist. *Nutrients*. 2019;**11**:2003. DOI: 10.3390/nu11092003
- [127] Lee MC, Hsu YJ, Ho HH, Hsieh SH, Kuo YW, Sung HC, et al. *Lactobacillus salivarius* subspecies salicinius SA-03 is a new probiotic capable of enhancing exercise performance and decreasing fatigue. *Microorganisms*. 2020;**8**:545. DOI: 10.3390/microorganisms8040545
- [128] Cox AJ, Pyne DB, Saunders PU, Fricker PA. Oral administration of the probiotic *Lactobacillus fermentum* VRI-003 and mucosal immunity in endurance athletes. *British Journal of Sports Medicine*. 2010;**44**:222-226. DOI: 10.1136/bjism.2007.044628

- [129] Michalickova D, Minic R, Dikic N, Andjelkovic M, Kostic-Vucicevic M, Stojmenovic T, et al. *Lactobacillus helveticus* Lafti L10 supplementation reduces respiratory infection duration in a cohort of elite athletes: A randomized, double-blind, placebo-controlled trial. *Applied Physiology, Nutrition and Metabolism*. 2016;41:782-789. DOI: 10.1139/apnm-2015-0541
- [130] Strasser B, Geiger D, Schauer M, Gostner JM, Gatterer H, Burtscher M, et al. Probiotic supplements beneficially affect tryptophan-kynurenine metabolism and reduce the incidence of upper respiratory tract infections in trained athletes: A randomized, double-blinded, placebo-controlled trial. *Nutrients*. 2016;8:752. DOI: 10.3390/nu8110752
- [131] Salarkia N, Ghadamli L, Zaeri F, Sabaghian RL. Effects of probiotic yogurt on performance, respiratory and digestive systems of young adult female endurance swimmers: A randomized controlled trial. *Medical Journal of the Islamic Republic of Iran*. 2013;27:141-146
- [132] Carbuhn AF, Reynolds SM, Campbell CW, Bradford LA, Deckert JA, Kreutzer A, et al. Effects of probiotic (*Bifidobacterium longum* 35624) supplementation on exercise performance, immune modulation, and cognitive outlook in division I female swimmers. *Sports*. 2018;6:116. DOI: 10.3390/sports6040116
- [133] Marshall H, Christmas BCR, Suckling CA, Roberts JD, Foster J, Taylor L. Chronic probiotic supplementation with or without glutamine does not influence the eHsp72 response to a multi-day ultra-endurance exercise event. *Applied Physiology, Nutrition and Metabolism*. 2017;42:876-883. DOI: 10.1139/apnm-2017-0131
- [134] Pugh JN, Sparks AS, Doran DA, Fleming SC, Langan-Evans C, Kirk B, et al. Four weeks of probiotic supplementation reduces GI symptoms during a marathon race. *European Journal of Applied Physiology*. 2019;119(7):1491-1501. DOI: 10.1007/s00421-019-04136-3
- [135] Inoue T, Kobayashi Y, Mori N, Sakagawa M, Xiao JZ, Moritani T, et al. Effect of combined bifidobacteria supplementation and resistance training on cognitive function, body composition and bowel habits of healthy elderly subjects. *Beneficial Microbes*. 2018;9:843-853. DOI: 10.3920/BM2017.0193
- [136] Townsend JR, Bender D, Vantrease WC, Sapp PA, Toy AM, Woods CA, et al. Effects of probiotic (*Bacillus subtilis* DE111) supplementation on immune function, hormonal status, and physical performance in division I baseball players. *Sports*. 2018;6:70. DOI: 10.3390/sports6030070
- [137] Toohey JC, Townsend JR, Johnson SB, Toy AM, Vantrease WC, Bender D, et al. Effects of probiotic (*Bacillus subtilis*) supplementation during offseason resistance training in female division I athletes. *Journal of Strength and Conditioning Research*. 2020;34(11):3173-3181. DOI: 10.1519/JSC.0000000000002675
- [138] Ibrahim NS, Muhamad AS, Ooi FK, Meor-Osman J, Chen CK. The effects of combined probiotic ingestion and circuit training on muscular strength and power and cytokine responses in young males. *Applied Physiology, Nutrition and Metabolism*. 2018;43:180-186. DOI: 10.1139/apnm-2017-0464