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MINI-REVIEW

Capacity of lactic acid bacteria in immunity enhancement and cancer prevention

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Abstract Lactic acid bacteria are associated with the human gastrointestinal tract. They are important for maintaining the balance of microflora in the human gut. An increasing number of published research reports in recent years have denoted the importance of producing interferon-gamma and IgA for treatment of disease. These agents can enhance the specific and nonspecific immune systems that are dependent on specific bacterial strains. The mechanisms of these effects were revealed in this investigation, where the cell walls of these bacteria were modulated by the cytokine pathways, while the whole bacterial cell mediated the host cell immune system and regulated the production of tumor necrosis factors and interleukins. A supplement of highly active lactic acid bacteria strains provided significant potential to enhance host's immunity, offering prevention from many diseases including some cancers. This review summarizes the current understanding of the function of lactic acid bacteria immunity enhancement and cancer prevention.

Keywords Lactic acid bacteria · Immunity · Cancer

Introduction

The gastrointestinal tract (GIT) microflora plays a crucial role in maintaining the health status of humans and animals. The importance of GIT microflora in the health of their host was first postulated by Metchnikoff at the beginning of the twentieth century (Underhill et al. 2016). He indicated that the human longevity might be increased by the consumption of lactic acid bacteria. However, GIT microflora was considered to be a harmful factor at that time, which overlooked their potential beneficial effects. Microbes used in yogurt products were considered as the sole source of GIT microflora at that time. Since then, much effort has been conducted to improve the beneficial influence of intestinal microflora to modulate the health of the host. This modulation was affected by the supplement of live microbes to the host normally known as probiotics. The probiotics are the microbes that induced benefit on the health of host by modifying gut microbiota. The goal of the supplement of these probiotics is mainly to enhance the immunity of their hosts (Sartor 2004; Wang et al. 2015). Lactic acid bacteria participate in a synbiotic relationship with their hosts and play a major role in the health of their hosts by preventing the overgrowth of pathogenic microbes and extracting the nutrient and energy from diets. The pathways linking the lactic acid bacteria and its hosts are through the metabolism, regulation of gene transcription, signaling cascades, and immune system (Chen et al. 2012; Lozupone et al. 2012; Turner et al. 2013).

After two decades of development, yogurt and fermented milk products have been listed as probiotic resources as a result of the identification of their beneficial effects on human health. At present, the genera *Lactobacilli* and *Bifidobacteria* have been recognized as the best probiotic microbes. Currently, these probiotic bacteria have been widely used as important sources for the development of practical foods. The healthy gut microflora has also proved to be capable of preventing diseases caused by gastrointestinal flora (Chen et al. 2016; Daly and Davis 2008; Quigley 2013).

At present, *Lactobacillus*, *Bifidobacteria*, *Enterococcus*, and algae have been listed as useful probiotics. Various

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Lactobacillus and *Bifidobacteria* species have been successfully used to reduce some gastrointestinal infections. These probiotics have been found to have the ability to produce vitamin B; stimulate immune response, cholesterol reduction, and anti-oxidant potential; and prevent ulcers, GIT tract infections, diabetes, and heart disorders (Chen et al. 2015; Clarke et al. 2012). In addition, these probiotic microbes were also found to stimulate the growth of beneficial microbes and suppress the growth of harmful microorganisms, modulate the defense mechanisms of the host, enhance the availability of nutrients, and reduce lactose intolerance (Kumar et al. 2009a; Kumar et al. 2010; Kumar et al. 2009b; Kumar et al. 2012; Nagpal et al. 2012; Yadav et al. 2007).

With the advancement of understanding, the importance of gut microflora to human health has continued to be revealed and identified at the level of genetics, immunity, and nutrition.

Selection of probiotic strains

Functionality and safety are the two essential criteria for selection of efficient probiotic microbial strains. At present, the most beneficial probiotic bacteria have been isolated from human beings (Guarner and Malagelada 2003). The major factors that should be considered for the selection of probiotic strains include the original human strain that is non-pathogenic in nature and lacks antibiotic resistance genes (Collins et al. 1998; Sornplang and Piyadeatsoontorn 2016). In addition, bile tolerance, acid tolerance, adherence to epithelial surfaces, immunomodulation, and anti-carcinogenic and antagonistic effects against pathogenic bacteria are the other major factors that should be consider in the functional evaluation of probiotic strains (Ohashi and Ushida 2009; Santos et al. 2016; Toma and Pokrotnieks 2006). In the final analysis, the selection of probiotic is an complicated issue, because the intestinal microbial flora is very complex in nature and has very specific characteristics (Haskard et al. 2001; Ishikawa et al. 2003). It is also not clear which type of intestinal microbial population is the principal one responsible for maintenance of human health (Ashraf and Smith 2016). Table 1 shows the currently reported beneficial effects and related mechanisms of probiotics.

Anti-cancer activity of lactic acid bacteria

Some lactic acid bacteria strains have been found to have activity in inhibiting colon cancer, liver cancer, lung cancer, and colorectal cancer in vivo or in vitro. Table 2 shows the potential of lactic acid bacteria as probiotics for prevention of the initiation of cancer.

Colon cancer Goldin and Gorbach (1984) found that consumption of a diet that included *Lactobacillus acidophilus* NCFM reduced the incidence of colon cancer in rats. The diet and antibiotics lowered the production of carcinogens in the colon. *Lactobacillus* GG was found to reduce the concentration of these carcinogenic enzymes and secondary bile salts, as well as reduce the absorption of mutagens that cause cancer in the colon (Drisko et al. 2003; Khan et al. 2013; Verma and Shukla 2013). A diet containing *Bifidobacterium longum* has been found to lower the expression of the ras-p21 genes and exhibit a strong inhibition against colon tumors (Cho et al. 2014; Reddy 1999).

Liver cancer The consumption of aflatoxin B1 (AFB1)-contaminated foods is the major cause of liver cancer, because it has been found to induce abnormal changes in the genetics of

Table 1 Health-promoting effect of probiotic bacteria and their mechanisms

Health benefit of probiotic microbes	Mechanisms	References
Enriched nutrient	Cofactor and vitamin production	Park and Oh (2007)
Resistance to pathogens	Antagonistic activity, enhance antibody production	Muñoz-Atienza et al. (2013)
Modulation of immune system	Enhanced the production of anti-inflammatory cytokine, strengthen the antigen-specific and antigen-non-specific immune response against infection	Tsai et al. (2012)
Urogenital infection	Competitive exclusion	Even et al. (2014)
Allergy	Suppressed immunologic reactions, prevent antigen translocation in blood	Randazzo et al. (2015)
Heart disease	Anti-oxidative effect, BSH activity, and cholesterol assimilation	Wang et al. (2014b)
Cancer	Enhance immune system, detoxification of carcinogens, anti-mutagenic ability	Zhong et al. (2014)

Table 2 Lactic acid bacteria with anti-tumor potential

Lactic acid bacteria	Function	References
B. adolescentis ATCC 15703VSL#3	Anti-mutagenic activity against mutagens, regulate the expression of COX-2	Chalova et al. (2008); Otte et al. (2008)
L. reuteri	Modulation of NF-κB and MAPK signaling pathways	Iyer et al. (2008)
L. paracasei F19	Induce IL-8 and IL-10	Kruszewska et al. (2002)
P. pentosaceus 16:1	Anti-oxidant ability	Kruszewska et al. (2002)
L. plantarum JCM 1551, *L. plantarum* KLAB21, *L. plantarum* 2592, *L. plantarum* L-137	Induce IL-12 and production of anti-mutagenic compounds	Ando et al. (2004); Khanafari et al. (2007); Murosaki et al. (2000); Rhee and Park (2001)
B. lactis	Prevent azoxymethane-induced cancer	Femia et al. (2002)
B. infantis	Anti-proliferative activity	Biffi et al. (1997)
L. delbrueckii	Increase expression of IL-8	Rafter (1995)
B. polyfermenticus	Reduce DNA damage and anti-oxidative ability	Park et al. (2007)
B. longum ATCC 15708	Anti-oxidative ability, reduced binding of carcinogen	Lin and Chang (2000); Vanderhoof (2001)
Lactobacillus GG	Regulate the expression of gene	Di Caro et al. (2005); Drisko et al. (2003); Femia et al. (2002)
L. casei Shirota	Inhibit IL-6	Matsumoto et al. (2009)
L. acidophilus	Reduce binding of carcinogen	Haskard et al. (2000)
S. thermophilus	Reduced DNA damage	Pool Zobel et al. (1996)

the ras proto-oncogenes and p53 tumor suppressor genes. Some lactic acid bacteria have been shown to bind to AFB1 and neutralize it, which can reduce the absorption of toxins from the gut to the cells (Abbes et al. 2016; Haskard et al. 2000). The addition of *Lactobacillus* GG to a diet can regulate the expression of genes related to cell adhesion, cell–cell signaling, cell differentiation, cell growth, apoptosis, tumor necrosis factor, and transforming growth factor-beta (Di Caro et al. 2005; Singh et al. 2014).

Lung cancer It has been reported that some lactic acid bacteria can prevent lung cancer by producing anti-mutagenic molecules, which alter the physiochemical conditions, thereby enhancing the immune system or enhancing the metabolic activity of the intestinal microbial populations (Hirayama and Rafter 2000).

Other cancers *Lactobacillus plantarum* 17C was found to have a strong anti-cancer effect against colorectal cancer cell HT-29 (Haghshenas et al. 2015). The combination of the increased diversity of vaginal microbiota with the reduction in *Lactobacilli* species is involved in the development of cervical cancer (Badiga et al. 2016; So et al. 2016). *Lactobacilli* has been suggested as a bacterium that is safe for human consumption and as a suitable candidate for drug delivery (Amrouche et al. 2006; Bezkorovainy 2001).

Mechanism of the anti-cancer activity of lactic acid bacteria

Inhibiting the growth or the carcinogenic enzyme production of adverse microbes Adverse gut microbes enhance the possibility of carcinogenesis by producing carcinogenic enzymes, which can convert procarcinogens into active carcinogens. The addition of *Lactobacillus casei* ATCC 39392 and *L. acidophilus* ATCC 4356 in a diet has been found to reduce the concentration of these carcinogenic enzymes, thereby suppressing their activities (Goldin 1990; Hosseini Nezhad et al. 2015). Some probiotic lactic acid bacteria can inhibit the growth of the microorganisms that produce carcinogenic enzymes such as beta-glycosidase, azoreductase, nitroreductase, and beta-glucuronidase (Kumar et al. 2012; Kumar et al. 2011; Reddy 1999).

Producing anti-mutagenic compounds *Bifidobacterium breve* (commercially available), *B. longum* (commercially available), *Streptococcus thermophiles* NCIM 50083, *Lactobacillus confuses* DSM2019, *Lactobacillus gasseri* P79, and *L. acidophilus* J71 have been found to exert strong anti-genotoxicity against *N*′-nitro-*N*-nitrosoguanidine (MNNG) and 1,2-dimethylhydrazine (DMH). Some strains of the *Pediococcus*, *Enterococcus*, *Leuconostoc*, *Lactococcus* and *Lactobacillus* species have been found to exert anti-mutagenic activity against a wide range of mutagenic compounds in vitro (Liang et al. 2016; Pierides et al. 2000; Solanki et al. 2015).

Degrading procarcinogens or inducing apoptosis in cancer cells The anti-carcinogenic capabilities of *lactic bacteria* also resulted from their ability to degrade procarcinogens (Lidbeck et al. 1992; Verma and Shukla 2013; Zhao and Shah 2016). The supplement of *Lactobacillus rhamnosus* LGG increased the expression of apoptosis-promoting genes p53, casp3, and bax (proapoptotic proteins) but reduced the expression of apoptosis-inhibiting genes tumor necrosis factor alpha (TNF-α), COX-2, and NF-κB-p65 in colon cancer cells (Gamallat et al. 2016).

Also, some compounds produced by lactic acid bacteria have cytotoxic activity against cancer cells or induce the apoptosis in cancer cells. Phenazine produced by *Lactococcus* BSN307 was found to have strong cytotoxic activity against cancer cells HeLa and MCF-7, but not against normal cell H9c2 (Varsha et al. 2016). The arginine deiminase exerted by *Enterococcus faecium* GR7 was observed to induce apoptosis in liver cancer cell HepG2 (Kaur and Kaur 2015). The anti-microbial peptides m2163 and m2386 produced by *L. casei* ATCC 334 showed activity to trigger apoptosis in cancer cell SW480 (Tsai et al. 2015). Fermenticin HV6b, a peptide produced by *Lactobacillus fermentum* HV6b MTCC 10770 isolated from human, possessed anti-tumor activity by inducing the apoptosis in HepG2 (Kaur et al. 2013).

Inhibiting the growth of cancer cells Ten of 138 *Lactobacilli* strains isolated from human infant feces were identified to have anti-proliferative activity against the HT-29 cells (Wang et al. 2014a). The composition of the cell wall in *Lactobacilli* strains was the major factor that induced apoptosis in the HT-29 cells through the mitochondrial pathways (Wang et al. 2014a). The exopolysaccharide produced by *L. plantarum* 70810 showed significant inhibition on the proliferation of cancer cell HT-29 and had potential in application as a natural anti-tumor drug (Wang et al. 2014a, b, c).

Enhancement of immunity by lactic bacteria

Lactic acid bacteria could establish a contact with the gut that was associated with lymphoid tissues that modulate the immune response of their hosts (Chen et al. 2015; Tsai et al. 2012). *Lactobacillus helveticus* R389, *L. rhamnosus* HN001, *L. acidophilus* HN017, and *B. longum* HY8001 (Hoseinifar et al. 2015; Inic-Kanada et al. 2016; Isolauri 2001; Kandasamy et al. 2016) have been reported to have the capability to enhance the immune system of their host. The mechanism of this enhancement is supposed to be caused by the effect of the lactic acid bacteria on the content of the following agents in their host: interferon-gamma, globulin, albumin, total serum protein, prostaglandin E production, tumor necrosis factor, interleukin-1 (IL-1), interleukin-2 (IL-2), interleukin-6 (IL-6), and lymphocytes proliferation, as well as increasing the amount of antibody-secreting cells, cytokine level, and phagocytic activity (Khan et al. 2013; Tsai et al. 2012; Zhao and Shah 2016).

Lactic acid bacteria and the non-specific immune system

Non-specific immune response is the first line in human defense against invading pathogens. It can be quickly activated by a variety of stimuli. The non-specific immune system consists of natural killer cells, leukocytes (such as neutrophils), and phagocytic cells (such as macrophages and monocytes). The phagocytosis reaction is initiated by various intracellular stimuli that can produce IL-1, tumor necrosis factor alpha, and nitrogen and reactive oxygen species (Choi et al. 2015; Rawlinson et al. 2000). IL-1 has been found to have a cytotoxic effect and inhibited the growth of colorectal cancer cell lines (Chen et al. 2013; Raitano and Korc 1993). Some strains of lactic acid bacteria have been found to enhance the activity of blood leukocytes and pulmonary and peritoneal macrophages, lysozyme secretion, and production of ROS and nitrogen species (LeBlanc et al. 2002; Perdigón et al. 2001; Sheih et al. 2001). *Lactobacillus kefiri* BCRC14011, *Lactobacillus kefiranofaciens* BCRC16059, *L. kefiranofaciens* M1, *L. kefiri* M2, *Leuconostoc mesenteroides* M3, and *Lactococcus lactis* M4 and the supernatant of their milk cultures exhibited high activity to induce the production of interleukin-12 (IL-12), IL-6, IL-1, and tumor necrosis factor alpha in mice macrophage cell RAW 264.7 in vitro (Hong et al. 2009; Jeong et al. 2015).

Experiments in mice Many studies have been conducted in animals and demonstrated the function of phagocytic cells varying between various lactic acid bacteria strains. Mice fed the fermented milk containing *L. casei* CRL 431 had higher secretions of lysozyme enzymes from the phagocytic cells than those fed *L. acidophilus* CRL 730, *Lactobacillus delbrueckii* ssp. *bulgaricus* CRL 423, and *Streptococcus thermophilus* CRL 412 (Giri et al. 2013; Perdigon et al. 2002). Studies showed the mice supplemented with probiotic lactic acid bacteria strains decreased the severity of inflammation and increased the expression of interleukin-10 (IL-10) and IL-17 (Del Carmen et al. 2014; Srutkova et al. 2015; Toumi et al. 2014). *L. plantarum* GBLP2 isolated from Korean fermented vegetable exhibited preventive effect against the influenza virus infections in mice (Kwak et al. 2016).

Experiments in fish Significant upregulation of IL-2, interleukin-7 (IL-7), interleukin-15 (IL-15), interleukin-21 (IL-21), IL-10, interleukin-1β (IL-1β), IL-6, TNF-α, and IFN-γ was observed in Japanese pufferfish treated with

Lactobacillus paracasei spp. *paracasei* (06TCa22) isolated from Mongolian dairy products (Biswas et al. 2013). A diet containing the mixture of *L. plantarum* FGL0001 from end gut of the olive flounder and *Lc. lactis* BFE920 from bean sprouts exhibited significant effects on the innate immune system. Ingestion of this type of diet can significantly protect against various diseases and can stimulate the immune system of the olive flounder, which was shown by the enhancement of the phagocytic activity of the innate immune cells, the neutrophil level, and lysozyme activity of skin cells. In addition, feeding flounder with probiotics also enhanced the expression of IL-8, IL-6, and tumor necrosis factor alpha. Also, *Lc. lactis* BFE920 was found to improve the survival rate, growth rate, and innate immune system of flounder previously infected with *Streptococcus iniae* (Beck et al. 2015; Beck et al. 2016; Van Doan et al. 2016).

Experiments in piglet Laboratory piglets treated with *L. casei* CRL 431 and *Streptococcus faecium* SF68 showed higher levels of IL-2 in ileal tissue and increased activity of phagocytic cells. The difference in the cell wall compositions of different *Lactobacilli* strains was the major factor responsible for these varied reactions. The *Lactobacilli* strains that adhere to the intestinal membrane and survive in the GIT tract tend to enhance the activity of phagocytic cells (Benyacoub et al. 2003; Perdigon et al. 2002).

Experiments in cell lines Salinas et al. (2008) found that *L. delbrueckii* subsp. *lacti*s CECT 287 had a stronger influence on the growth of fish cell lines SAF-1 and EPC than other strains in the same species. *B. longum* 1941, *Bifidobacterium animalis* subsp. *lactis* BB12, and *B. breve* BB99 increased the expression of IL-4, IL-10, and TGF-beta and *L. casei* 290, *S. thermophilus* M5, *Lc. lactis*, and *L. rhamnosus* G5435 induced the production of proinflammatory cytokines by T cells (Ashraf et al. 2014). *Lactobacillus salivarius* B-30514, *Lactobacillus reuteri* 132, and *L. acidophilus* 88 are all found naturally in chicken intestines. A supplement of the supernatant of these *Lactobacilli* species in live cells was found to enhance the expression of IL-1 beta (Brisbin et al. 2010; Gong et al. 2007; Plaza-Diaz et al. 2014). *L. salivarius* JTB07 and *L. reuteri* JTB07 have been reported to upregulate the expression of IL-12, IL-8, IL-6, and IL-1, while *L. acidophilus* JTB05 to upregulate the interferon-gamma expression level of their host cells (Quinteiro-Filho et al. 2015). *L. salivarius* UCC 118 and *Lactobacillus johnsonii* LJ-1 were reported to increase the IgA response and phagocytic activity in head-kidney leucocytes. The modulation of the immune response by these two strains was not associated with any potential harmful effect and even offered some beneficial effect (Munoz-Atienza et al. 2015).

Interaction between lactic bacteria and its hosts The inflammatory response cytokine that can activate macrophages and monocytes was also enhanced during the interaction between lactic acid bacteria and their hosts, which resulted in the production of some toxic compounds related to the lysis of cancerous cells (Khan et al. 2013; Tsai et al. 2012; Zhao and Shah 2016). IL-6-CKS9 is a novel recombinant cytokine generated by conjugating the IL-6 and M cells targeting peptides, and it facilitates the enhancement of mucosal immune response of host cells. The recombinant *Lc. lactis* IL1430 was developed to be a host to secrete and express IL-6-CKS9 for mucosal vaccine adjuvant. *Lc. lactis* IL1430 was orally administered to mice along with the model antigens protein and showed consistent enhancement tendencies in mucosal and systematic immune response (Chen et al. 2013; Li et al. 2015). The mice treated with *L. gasseri* TMC0356 showed enhancement in IL-6, IL-10, and IL-12 productions and phagocytic activity as compared to the control (Yoda et al. 2014).

Practical application of lactic acid bacteria Lactic acid bacteria are becoming more important in aquaculture to increase production. The most popular bacteria used for this purpose include *Leuconostoc*, *Lactococcus*, and *Lactobacillus*. The dietary supplementation with lactic acid bacteria, either a single species or a mixture, can enhance the expression of cytokine, phagocytic activity, and lysozyme activity in fish aquaculture (Lazado and Caipang 2014; Nayak 2010). In addition, oral administration of lactic acid bacteria was found to stimulate the activation of the cytotoxic activity of natural killer cells and macrophage cells (Chang et al. 2015; Matsuzaki 1998; Zhao et al. 2015). A cell-free culture (CFC) of *L. salivarius* JTB07 enhanced the expression of IL-1, interferon-gamma, and IL-8 in the host cells, whereas other *Lactobacillus* strains did not. *L. plantarum* HOKKAIDO decreased the neutrophil ratio and increased the lymphocyte ratio when compared with the control group (Nishimura et al. 2015). Feeding heat-killed lactic acid bacteria was also tried in animals. In mice, heat-killed *L. plantarum* strain L-137 was a more potent inducer of IL-12 than other heat-killed *Lactobacillus* strains. The mechanism was that this strain possesses a higher efficiency of phagocytosis for the potent IL-12 p40 induction (Murosaki et al. 2000; Hatano et al. 2015). Heat-killed *L. plantarum* enhanced non-specific immune defense system of red sea bream, providing them with higher resistance to the stress and better immune response (Dawood et al. 2015).

Lactic acid bacteria and specific immune system

The specific immune system has two categories: cellular immunity and humoral immunity. Cellular immunity is initiated by T lymphocyte, and humoral immunity is initiated by the antibodies produced by plasma cells such as lymphocyte.

Gut infection Many studies have shown that lactic acid bacteria can protect hosts against various gut infections (Saavedra et al. 2004; Tohno et al. 2007), such as *E. coli*, *Salmonella*, and *Shigella*. A gnotobiotic rat group fed *E. coli* together with *L. plantarum* had a lower amount of *E. coli* than those only fed *E. coli* (Even et al. 2014; Guarner and Malagelada 2003; Haskard et al. 2001; Ishikawa et al. 2003; Kailasapathy and Chin 2000; Kalliomäki et al. 2001; Kankaanpää et al. 2001; Leroy and De Vuyst 2004). Also, a rat group fed *L. plantarum* showed higher levels of IgA and IgM antibodies against *E. coli* than the control group. *L. casei* strain Shirota has been found to protect its hosts against *Salmonella typhimurium* by increasing the level of IgA-secreting cells and the level of IgA in gut fluids (Harbige et al. 2016; Shida et al. 2015; Villena et al. 2005). Mice fed fermented milk containing lactic acid bacteria were found to develop resistance against *Shigella* infection by producing anti-*Shigella* antibodies in blood serum (Maldonado et al. 2012). In human, clinical reports showed that the consumption of fermented food containing lactic acid bacteria could reduce the risk of allergy development via modulation of the immune system. The consumption of this type of fermented milk was also found to enhance the production of type I and type II interferons (Mattila-Sandholm et al. 2002; Saarela et al. 2000; Shaheen et al. 2015; Yang 2015; Yang et al. 2015). These results illustrate that mammals fed *Lactobacilli* can exhibit enhanced specific and non-specific immune responses and produce high level of antibodies (Herias 2001). However, due to oral tolerance, the initiation of a specific immune response by supplementing a diet with lactic acid bacteria is not remarkable (Perdigón et al. 2001; Saez-Lara et al. 2015).

Cellular immunity After contact with antigens, the T lymphocyte cells produce cytokines, which proliferate and thereby enhance the activity of other immune cells (Tizard 2000). In animal models, lactic acid bacteria were found to reduce the risk of allergies by enhancing the production of IL-4 and IL-5 in animals. Recent research has shown that lactic acid bacteria can also induce the production of IL-12 and IL-18 and stimulate secretion of cytokines by interaction with phagocytic cells via the NF-κB and STAT signaling pathways (Cross et al. 2001; Lin et al. 2016). The consumption of *Lactobacilli* and *Bifidobacteria* showed significantly increased protection in mice against intracellular bacterial pathogens and tumor growth (Gutiérrez et al. 2016). These results suggested that lactic acid bacteria enhance cell-mediated immunity by increasing the lymphocyte cell proliferation, mononuclear cell phagocytic capacity, and tumoricidal activity of natural killer cells (Fong et al. 2015; Lin et al. 2016; Shu et al. 2000).

Humoral immunity The cell wall and cytoplasm components of *Bifidobacteria* have been found to have stronger effect on cell proliferation and cytokine production of splenocyte cell, whereas the exopolysaccharide of the bacteria had no such effect (Amrouche et al. 2006; Živković et al. 2016). However, exopolysaccharide-producing *Bifidobacteria* exhibited good adherence to HT-29 and Caco-2 cell lines and stimulated the proliferation and cytokine production of blood mononuclear cells (Serafini et al. 2013). The supernatant isolated from the biofilms formed by *L. plantarum* WCFS1 and *L. fermentum* CRL 1058 has been found to suppress the tumor necrosis factor alpha production (Aoudia et al. 2016; Chen et al. 2016; Salinas et al. 2008). Oral administration of *L. helveticus* HY7801 prevented the development of arthritis in human by reducing the level of inflammation and IgG, initiating the $CD11c^+$ dendritic cells and thus suppressing the production of proinflammatory cytokine, and enhancing the production of anti-inflammatory cytokines by T cells (Kim et al. 2015).

The *Lc. lactis* can also be considered as an alternative vector to deliver heterologous antigen to the bird immune system (Kobierecka et al. 2016). The oral administration of *Pediococcus acidilactici* DSPV006T, *L. salivarius* DSPV315T, and *L. casei* DSPV318T increases calf's ability to response to diseases by increasing the systematic immune response (Soto et al. 2016). The recent investigation showed that some endogenous lactic acid bacteria strains had effects on the immunity in bees during the larval stage, indicating that the response of bees to endogenous lactic acid bacteria is specific at levels of immune and species (Janashia and Alaux 2016).

Conclusions

Lactic acid bacteria play an important role in cancer etiology because they can influence many features of the intestinal tract such as physiology, immune homeostasis, metabolism, and development. Although laboratory-based studies have verified that lactic acid bacteria possess strong anti-tumor effects and benefits, it should not be blown up before we get more results from clinical trials in human. This is very essential before the medical community can admit the use of lactic acid bacteria as an alternative cancer control.

Lactic bacteria also play an important role in the protection and improvement of immunity in animals. The presence of lactic bacteria in the gut can protect the host from pathogens by competition for the adhesion place and substrates. Any disturbance can enhance the growth of harmful bacteria, which can induce diseases. The beneficial microbes have a positive effect on the host's immune system and protect the host from binding of pathogen microbes to mucous membranes, which maintains the balance between lymphoid cells and gut microflora. The related mechanisms of antagonism and immunity are related to changes in the composition of beneficial bacteria in the GIT tract. Lactic acid bacteria can enhance the immune system of the host by improving the innate immunity through receptors of regulated pathways and modulate the immune system by increasing the number of epithelial cell and immune cell while enhancing the production of IgA and interferon-gamma.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

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