REVIEW ARTICLE

Probiotics and Disease: A Comprehensive Summary—Part 9, Cancer

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Abstract

This article provides a literature review of the disease-specific probiotic strains associated with cancer. The literature review was restricted to research in both humans and animals. This is not an exhaustive review. The table design allows for quick access to supportive data and will be helpful as a guide for both researchers and clinicians. The goal of the probiotics and disease series is to provide clinically useful tools. The first article part 1 focused on mental health and neurological conditions; the second article part 2 explored cultured and fermented foods that are commonly available in the United States; part 3 explored the relationship between bacterial strains and 2 of the most prevalent diseases we have in modern society: cardiometabolic disease and fatigue syndromes; part 4 elucidated the role of the microbiome in infectious diseases; part 5 explored respiratory conditions of the ears, nose, and throat; part 6 explored the relationship between microbiota and skin disorders; part 7 reviewed allergy and autoimmune disease; and part 8 examined gastrointestinal and genitourinary conditions. This ninth article reviews the relationship between microbiota and cancer development and prognosis. This literature review is specific to disease condition, probiotic classification, and individual strain.

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The purpose of this summary is to provide nutritionists and other medical practitioners with a reference guide for recommending health-promoting, commercially produced, cultured and fermented food products to patients. There is considerable research on the gut microbiome and role of probiotics; however, this research has not been clearly connected with clinical practice. The authors undertook a review of current literature to explore which specific probiotics and probiotic strains have been utilized in clinical and laboratory studies.

To make this clinically valuable, product names of probiotics and fermented foods have been included. Finished products vary between manufacturers; thus, the researchers included brand listings to provide transparency and to facilitate a functional probiotics guide for clinicians. Exclusions of products meeting our criteria do not imply that these products are not effective—we simply were not aware of them.

Methodology

This literature review originated from a group project that was part of the requirements for a course in the doctoral program in functional and clinical nutrition at Maryland University of Integrative Health (Laurel, MD, USA). The student researchers had approximately 2 months to review the literature and synthesize the paper. The authors agreed on format, templates, and execution. Each author researched and wrote sections reviewing probiotics in relation to various health conditions with

literature searches conducted in PubMed, Biomed Central, EBSCO Research Premier, PLoS One, Cochrane reviews, and topic-specific open-source journals.

The review of specific probiotic products in the professional marketplace and specific probiotics products was performed using Internet searches, primarily Shop Google, in addition to topic specific databases to search for specific probiotic species including the strains listed in the research. Novel strains were cross-referenced to determine whether the strain was available only for research purposes. If a probiotic combination was used in the research, formulas that closely matched the combination were included. Formulas that contain all or most of the specific probiotics and strains were also included. The food survey focused on bacterial strains in food and includes foods that are commercially produced and commonly available in the refrigerated sections of grocery stores in the United States. Information was gleaned from commercial Web sites, communications with food company personnel, and by visiting grocery stores (primarily in California).

Research Overview: Cancer

Cancer incidence and mortality have been steadily increasing worldwide in this past century, emphasizing its role as a public health crisis. As a result, practitioners are searching for innovative approaches to reduce the burden cancer has on society. Cancer is a complex disease that includes abnormal proliferation of damaged cells that produce neoplasms with metastatic potential. Within individual tumors, there can be several subtypes of metabolic cells, each requiring a different treatment approach. Effectively, this means that by treating 1 subtype of cell within the tumor, there could be growth in another.[1]

Probiotics have been used for decades to promote a healthy microbiome. However, until recently, there have been limited clinical trials proving efficacy, especially in relation to complex diseases such as cancer. Evidence suggests certain strains of probiotics may even enhance the immune response providing a novel approach for cancer prevention and/or treatment.[2] Recent studies indicate that certain species of probiotic bacteria may reduce the risk, incidence, and number of tumors of the colon, liver, and bladder.[2]

As one might expect, the effects of probiotics in colorectal cancer has been studied extensively. Chen et al[3] found that *Clostridium butyricum* and *Bacillus subtilis* inhibited the proliferation of colorectal cancer cells, caused cell cycle arrest and promoted apoptosis. The molecular mechanism involved reduced inflammation and improved immune homeostasis. This work establishes a basis for the protective role of the probiotics *B subtilis* and *C butyricum* in intestinal tumorigenesis.[3] Lee et al4 found that the anti-inflammatory effect of *Lactobacillus lactis* NK-34 was demonstrated by decreased levels of nitric oxide production and proinflammatory cytokines. These results suggest that *L lactis* NK-34 could be used as a probiotic microorganism for its anticancer and anti-inflammatory effects.[4] Donaldson[5] stated that lactic acid producing species including *Lactobacillus* species and *Eubacterium aerofaciens* conferred a lower risk of colon cancer, whereas *Bacteroides* and *Bifidobacterium* species were associated with higher risk. Furthermore, probiotic species produce short chain fatty acids in the colon increasing acidity which is also associated with decreased colon cancer risk.[5]

Approximately 90% to 95% cancers are due to lifestyle factors, environmental toxins, and infections, and the remaining 5% to 10% are due to genetics.[6] These environmental factors are especially salient when reviewing colon cancer risk.[2] Research has explored the role of probiotics in colon cancer prevention, but not necessarily colon cancer remediation. New research shows that the microbiome contributes to colon cancer through the initiation of the inflammasome.[2] Inhibition of colon carcinogenesis was also noted due to a stimulated growth of *Bifidobacteria* in the colon. Ingestion of *Bifidobacterium longum* via dietary supplements was shown to provide significant suppression in tumor multiplication as well as a decrease in the size of tumor volume. This relationship suggest that probiotics may remediate as well as prevent the risk of colon cancer.[2]

Goldin et al[7] explored the use of *Lactobacillus* GG in a rat model of intestinal tumors. The authors found *Lactobacillus* GG reduced the levels of fecal enzymes such as beta-glucuronidase, azoreductase, nitro-reductase, and urease, which are responsible for catalyzing the conversion of carcinogenic amines. Bazzan et al[8] elucidated how microbiota may prevent or retard neoplastic growth by regulating the function of the gut immune response. Probiotic bacteria can produce metabolites such as conjugated linoleic acid (CLA), a polyunsaturated fatty acid that has anticarcinogenic effects.8 In a murine model, a study compared CLA to VSL#3, a probiotic containing 450 billion bacteria (*Streptococcus thermophilus*, *Bifidobacterium breve*, *B longum*, *Bifidobacterium infantis*, *Lactobacillus acidophilus*, *Lactobacillus plantarum*, *Lactobacillus paracasei*, and *Lactobacillus delbrueckii* spp *bulgaricus*). According to Bazzan et al,[8] "Both CLA and VSL#3 suppressed colon carcinogenesis, although VSL#3 showed greater anticarcinogenic and anti-inflammatory activities than CLA [alone]. CLA modulated expression of COX-2 levels in the colonic mucosa, whereas VSL#3 targeted regulatory mucosal CD4+ T cell responses." In addition, Bazzan et al[8] touted the benefit of prebiotic fibers including inulin and fructooligosaccharides, which are important for growth and proliferation of the microbiome. Intake of foods high in these prebiotics may, therefore, be used to help prevent or reduce the occurrence of certain forms of cancer.

In a study by Vyas et al,[9] it was shown that polypectomized and colon cancer patients treated with probiotics had increased *Lactobacillus rhamnosus* and *Bifidobacterium lactis* in their feces, along with reduced

amounts of *Clostridium perfringens*. This bacterial shift prevented increased secretion of interleukin (IL) 2 in polypectomized patients and increased production of interferon-γ in cancer patients.[9] Furthermore, an article by Zhong et al[10] elucidated the roles of lactic acid bacteria in colorectal cancer prevention. These lactic acid bacteria may induce apoptosis, playing a critical role in the prevention of colorectal cancer. *Lactobacillus reuteri* may also help prevent colorectal cancer by the downregulation of nuclear factor-kappa B (NF-κB), which can influence NF-κB-dependent gene products used in the regulation of cell proliferation including COX-2 and cyclin D1, as well as cell survival via Bcl-2 and Bcl-xL.[10] A component of *L acidophilus* and *L rhamnosus* called exopolysaccharides may help provide an antitumorigenic effect against HT-29 colon cancer cells by activating autophagic cell death by promoting the induction of Beclin-1, GRP78, Bcl-2, and Bak.[10] Lactic acid bacteria may additionally be used as chemotherapeutic adjuvants as *L acidophilus* and *Lactobacillus casei* appear to improve apoptosis-induction capacity of 5-flourouracil in colorectal carcinoma cell line LS513.[10] Lactic acid bacteria may also work via antioxidation. *B longum* and *L acidophilus* appear to inhibit linoleic acid peroxidation by 28% to 48%, showing that lactic acid bacteria may help prevent oxidative DNA damage in colon cells.10 In the immune system, lactic acid bacteria such as *L acidophilus* provide stimulation to the innate immune system, allowing for production of inflammatory and regulatory cytokines that then stimulate dendric cells (DCs) to produce IL-12 and IL-10. In fact,

> Reinforcing the roles of [lymphotoxin-alpha, also known as tumor necrosis factor-beta] (LTA), studies using LTA-deficient *L acidophilus* (NCK2025) strain led to normalization of innate and adaptive pathogenic immune responses and caused regression of established colonic polyps. Not only IL-12 and TNF-α were down-regulated by NCK2025, but also IL-10 in DCs was significantly enhanced and CD4+ T-cells were activated. The mice acquired significant protection from colitis with increased densities of effector Foxp3+RORγt- Tregs in response to oral administration of *L. acidophilus* NCK2025.[10]

Additional immune effects of lactic acid bacteria include enhancing the total numbers of T cells, natural killer cells, major histocompatibility complex II+ cells, and CD4-CD8+ T cells, as well as the induction of cytokines, such as interferon gamma, IL-1β, and tumor necrosis factor (TNF) alpha.[10]

Haghshenas et al[11] investigated *Lactobacillus* isolated from sheep dairy products including yogurt and ewe colostrum and found that these products contained 17 *Lactobacillus* strains including *L delbrueckii*, *L plantarum*, *L rhamnosus*, *L paracasei*, and *L casei*. These probiotics displayed a desirable tolerance to low pH and high concentrations of bile salts, favorable antipathogen activity, and acceptable antibiotic susceptibility. Thus, these strains should be considered therapeutic probiotics. In addition, *L plantarum* 17C, which is also found in sheep dairy products, showed significant antiproliferative effects on HT-29 human colon cancer cell line.[11]

There are also several epidemiological studies that support the protective role of probiotics against breast cancer.[2] Aragon et al[12] used different probiotic strains in mice to modulate the immune response in mammary neoplasia. Specifically, *L reuteri* ATCC-PTA-6475 and *L casei* CRL-431 were beneficial in decreasing tumor growth after detection. *L acidophilus* and *L casei* subspecies also promoted a significant decrease in tumor growth and prolonged survival in mice bearing invasive ductal carcinoma.[12] In a murine model, tumor volumes of mice treated with selenium nanoparticle-enriched probiotic were decreased while their survival rate increased compared with mice that received the probiotic alone or control mice in 4T1 breast cancer bearing mice.[12] Furthermore, there was a significant decrease of tumor growth in 4T1 tumor bearing mice due to modulation of the host's immune response by *L acidophilus* isolated from traditional homemade yogurt and from neonatal stool.[12] Reddy et al[13] reported that feeding yogurt to Swiss mice results in a 28% to 35% reduction in Ehrlich ascites tumor cells when compared with control groups fed milk.

Although these results are exciting advancements for breast cancer treatment, "there is no direct experimental evidence for cancer suppression in human subjects as a result of the consumption of probiotic cultures in fermented or unfermented dairy products, but there is a wealth of indirect evidence based largely on laboratory studies."[2] The incidence rate for cervical cancer is 8.1 cases per 100 000 women per year in the United States, although only approximately 1 of every 1100 women will develop vaginal cancer in her lifetime.[14] When considering the immense bacterial richness in the vagina, it is plausible that probiotic modulation may offer some benefit. Cribby et al[15] found that vaginal neoplasia treated with *Lactobacillus* strains inhibited growth of urogenital pathogens and yeast biofilms. In a study of 120 children with persistent primary vesicoureteral reflux, *L acidophilus* treatment daily was as effective as trimethoprim/sulfamethoxazole in reducing the rate of urinary tract infections.[15] Similar results were observed years earlier utilizing a modified strain of *L casei* as an adjuvant immunotherapy agent with radiation therapy in the treatment of stage III cervical cancer.[16] Motevaseli et al[17] demonstrated that common vaginal *Lactobacilli* exert cytotoxic effects on cervical tumor cells, but not on normal cells, and that this cytotoxicity is independent of pH and lactate. Although further studies are needed, probiotic therapy could prove to be a positive intervention for vaginal and cervical cancer rates.

According to Tao et al,[18] probiotics may be helpful in the treatment of hepatocellular carcinoma by preventing progression by improving endotoxemia. Hepatocellular carcinoma (HCC) is typically a complication of liver

diseases such as viral hepatitis and liver cirrhosis and is heavily influenced by the microbiome.[18] The authors wrote,

> Alterations of the type and amount of gut microbiota not only promote gut flora balance, intestinal inflammation and mucosal barrier function, but also dramatically improve the cirrhotic condition and prevent the occurrence of HCC. Interestingly, probiotics could inhibit the translocation of endotoxin, which bears PAMPs, and activate the damage-associated molecular patterns (DAMPs) such as high mobility group box 1.[18]

Furthermore, there are abnormalities in these patients including increases in *Enterobacteriacae* and *Enterococcus* with decreased levels of *Bifidobacterium* species.[18]

A study by El-Nezami et al[19] showed that a probiotic supplement with a mixture of *L rhamnosus* LC-705 and *Propionibacterium freundenreichii* subsp Shermanii strains twice per day for 5 weeks reduced the biological dose of aflatoxin exposure and may offer an effective dietary approach to decrease the risk of hepatocellular carcinoma. Aflatoxin is a type of mycotoxin produced by *Aspergillus flavus* and *Aspergillus parasciticus*, which are both well-known human hepatocarcinogens and increase risk for this type of cancer when consumed in foods such as peanuts and grains.[19]

The role of microbiota in murine models of lung cancer was explored by Gui et al.[20] The authors looked at the role of the intestinal microbiota in Lewis lung cancer mice that had been treated with an antibiotic cocktail of vancomycin, ampicillin, and neomycin, allowing for the destruction of the commensal microflora. These mice had significantly larger tumors than mice that had only be treated with the single antibiotic cisplatin. More important, in mice treated with both cisplatin and *Lactobacillus* bacteria had even smaller tumors and improved survival rates.[20]

Donaldson[5] described 2 trials of patients with superficial bladder cancer and given the probiotic *L casei*. In the first of the trials, the group given the *L casei* had a 50% disease free time of 350 days, whereas the control group only had 195 days. The second trial also indicated that the probiotics were significantly better than placebo, except for patients with multiple recurring tumors.

Whether microbes directly or indirectly influence immune cells remains unclear; however, studies relate increased lymphocyte proliferation with abnormal DNA replication. This relationship suggests that the microbiome affects lymphomagenesis and, thereby, determines which bacterial strains cause, prevent, or increase the risk of lymphoma development, which could prove to be instrumental in the treatment of this disease. Hosoya et al[21] found *Lactobacillus helveticus* SBT-2171 inhibited the proliferation of lymphocytes through a suppression of the c-Jun N-terminal kinase (JNK) signaling pathway, exerting an immunosuppressive effect in vivo. Inoculation of mice with *Lactobacillus johnsonii* decreased measures of DNA damage, oxidative stress, and inflammation inhibiting lymphocyte proliferation.[22]

Enterococcus faecalis CECT-7121 is thought to have immunomodulatory properties by displaying antibacterial properties, having susceptibility to antibiotics, and does not express virulence factors such as haemolysin, gelatinase, lipase, Dnase, decarboxylase. or aggregation substances.[23] Leukemia and blood cancer (LBC) cells are "a poorly immunogenic cell line derived from a spontaneous murine T-cell lymphoma, which grows progressively and aggressively in a syngeneic host (BALB/c mice) as ascites or solid tumor. The intraperitoneal injection of LBC cells kills all animals in 18 days."[23] Castro et al[23] found that *E faecalis* CECT-7121 affected tumor growth via the downregulation of LBC cell proliferation, induction of apoptosis and by improving the immune response that protects against lymphoma.

Probiotics are used in leukemia for several reasons. As with any cancer, cachexia is quite common and often renders the patient too weak to survive traumatic treatments including chemotherapy and radiation. In a mouse study, *L reuteri* 100-23 and *Lactobacillus gasseri* 311476 were given to mice that were transplanted with BaF3 to cause cancer cells to grow in the liver and spleen.[24] As a consequence of tumor progression, the mice experienced loss of both fat and muscle (cachexia). Results suggested significant dysbiosis with mice showing normal total bacteria levels and *Bacteroides* species, yet compared with controls, *Lactobacilli* and *Bifidobacteria* levels were found to be reduced. This was particularly true for levels of *L johnsonii*, *L gasseri*, and *L reuteri*, which were all greatly reduced.[24] Supplementation with *L reuteri* and *L gasseri* was effective in reducing proinflammatory cytokines including IL-6 and TNF-α.[24] Although there were no changes in weight or leukemia progression, the probiotics did help to decrease T-helper cell 2 (Th_2) immunity, which may have contributed to decreased atrophy.[24]

In addition to using probiotic strains directly, prebiotics may also be helpful in managing and preventing cachexia. Use of pectic oligosaccharides (POS) helped improve the metabolic consequences of leukemia, which, in turn, prevented cachexia.[25] POS was found to decrease the diversity and richness of fecal microbiota but improved levels of *Bifidobacterium* species, *Roseburia* species, and *Bacteroides* species. *Bifidobacterium dorei* was also increased by POS use. Although the use of inulin was not found to be as effective as POS in preventing or mediating cachexia, its ability to produce the short chain fatty acids propionate and butyrate were found to decrease risk for liver metastasis.[25]

Certain probiotic species may also promote apoptosis on cancer cells found in leukemia. For example, *L casei* and *Lactobacillus rhamnoses* positively influence apoptosis in the human monocytic leukemia cell line, THP-1.[26] Children with leukemia have decreased richness and diversity of oral microbiota as compared with healthy controls. This is caused by immune system interactions with the microbiota caused by cancer as malignant

lymphocytes infiltrate the oral mucosa and affect oral immunity. As a result, there are changes in salivary secreted immunoglobulin (Ig) A, alpha-amylase, and lysozyme.[27] Similarly, a kefir grain product made using the probiotic *Lactobacillus kefiri* P-IF via fermentation technology could successfully induce apoptosis in human multidrug-resistant myeloid leukemia (HL60/AR) cells in vitro. Apoptosis was also caused by *L reuteri* ATCC-PTA-6475 in myeloid leukemia-derived cells. which were induced by TNF. This was accomplished via the downregulation of nuclear factor-κB-dependent genes that cause cell proliferation such as Cox-2 and cyclin D1, as well as cell survival via Bcl-2 and Bcl-xL.[28] Finally, *L plantarum* is thought to cause cytotoxic activity on promyelocytic leukemia cells as shown in an in vitro study.[29]

Avcin et al[30] described in a letter to the editor five case studies of cancer patients suffering from bacteremia of invasive *Bifidobacterium* species secondary to infection. A case of pediatric Philadelphia chromosome-positive acute B-cell lymphoblastic leukemia was shown to have invasive *B breve* causing sepsis. This caused abdominal discomfort and constipation that eventually led to food refusal, neutropenia, hypotension, thickened intestinal wall and fecal masses (as seen on ultrasonography).[30] This case concludes that caution must be used when recommending probiotics to cancer patients with chemotherapy-induced neutropenia.[30]

Scientists are developing multiple strains of probiotics that can alter the immune response and inhibit the growth of carcinogens and restore the microbiota to promote optimal health.[31]

Some of these probiotics are also being engineered to detect cancer. *Escherichia coli* Nissle 1917 (EcN) PROP-Z was developed at Massachusetts Institute of Technology and is designed to safely detect the presence of hepatic tumors via metabolomics in two models of liver metastasis.[31] By creating a noninvasive, low-cost diagnostic, practitioners can more easily monitor the progression and potentially regression of disease.

Table 1. Selected Types of Cancer

Cancer	Strains	Overview	Professional and Commercial Supplements	Foods
Leukemia				
Avcin et al[30] (2015)	*B breve*	Caution: In a letter to the editor, 5 suffering from bacteremia of invasive *Bifidobacterium* spp secondary to infection were described. A case of pediatric Philadelphia chromosome-positive acute B-cell lymphoblastic leukemia was shown to have invasive *B breve* causing sepsis.	Ther-Biotic Factor 4 (*Bifidobacterium* Complex) 60c, Klaire Labs (*B breve*)	*B breve* found in Yakult
Bindels et al[24] (2012)	*L reuteri* 100-23, *L gasseri* 311476	Mice that are transplanted with Ba-F4 cells which cause cancer cells to grow in the liver and spleen also cause the mice to lose fat and muscle. This results in intestinal dysbiosis. The mice had normal total bacteria levels and *Bacteroides* spp compared with controls; however, lactobacilli levels and bifidobacteria levels were reduced. Particularly levels of *L johnsonii/gasseri* and *L reuteri* were greatly decreased. *L reuteri* 100-23 and *L gasseri* 311476 given to BaF4 mice with leukemia resulted in decreased levels of proinflammatory cytokines (IL-6 and TNF-α) as well as decreased expression of muscle atrophy markers. However, this did not result in changes of weight or leukemia progression. The probiotics helped to decrease Th_2 immunity, which might have contributed to decrease atrophy.	Isolated for research purposes only.	None
Wang et al[27] (2014)	*L casei*	*L casei rhamnosus* positively influence apoptosis in the human monocytic leukemia cell line, THP-1. Note: Children with leukemia have decreased richness and diversity of oral microbiota as compared with healthy controls. This is caused by immune system interactions with the microbiota caused by cancer as malignant lymphocytes infiltrate the oral mucosa and affecting oral immunity. This causes changes in salivary secreted immunoglobulin A, α-amylase, and lysozyme.	PerioBiotic™ Toothpaste - Designs for Health (*L casei*) Mega Foods Mega Flora (*L casei*) Innate Flora 5-14 Complete Care (*L casei*)	Zukay Live Foods Veggie Kvass, Fruit Kvass; Amande cultured almond milk; Nancy's Organic cultured soy Dahlicious cow's milk lassi; Green Valley Organics lactose-free kefir; Springfield Creamery; Nancy's Organic low-fat plain kefir; Redwood Hill Farm goat milk kefir
Ghoneum & Gimzewski[26] (2014)	*L kefiri* P-IF	A probiotics fermentation technology kefir grain product using the probiotic *L kefiri* P-IF successfully induced apoptosis in human multidrug-resistant myeloid leukemia (HL60/AR) cells in vitro.	Isolated for research purposes only.	Kefir made from *L kefiri* P-IF via probiotics fermentation technology
Bindels et al[24] (2012)	*Bifidobacterium* spp, *Roseburia* spp, *Bacteroides* spp, *B dorei*	In a mouse-based leukemia study POS and inulin were used to improve metabolic consequences of leukemia preventing cachexia. POS, but not inulin, decreased the diversity and richness of fecal microbiota but improved levels of *Bifidobacterium* spp, *Roseburia* spp, and *Bacteroides* spp, *B dorei* was particularly increased by POS. In this way it positively affected a decrease in cachexia. Inulin increased short-chain fatty acids including propionate and butyrate, as well as decreasing liver metastasis.	Gr8-Dophilus NOW (*Bifidobacterium* spp) Garden of Life RAW for women (*Bifidobacterium* spp) Mega Foods Mega Flora/ Flora 5-14 Complete Care (*Bifidobacterium* spp) *Roseburia* spp *Bacteroides* spp and *B dorei* are not commercially available	Real Yogurt by Cultures for Health (*Bifidobacterium* spp)

Table 1. (continued)

Cancer	Strains	Overview	Professional and Commercial Supplements	Foods
Iyer et al[28] (2008)	*L reuteri* ATCC-PTA-6475	*L reuteri* ATCC-PTA-6475 appears to help induce apoptosis in myeloid leukemia-derived cells induced by tumor necrosis factor by downregulating nuclear factor-kB-dependent genes that cause cell proliferation (COX-2, cyclin D1) and cell survival (BCL-2, BCL-xL). *L reuteri* appears to help regulate the proliferation of cancer cells via the alteration of key protein levels by helping induce apoptosis and affecting the homeostasis of pro apoptotic and antiapoptotic factors in cells stimulated by tumor necrosis factor.	BioGaia Gastrus, Chewable Tablets, Mandarin Orange (*L reuteri* ATCC PTA 6475)	None
Puertollano et al[29] (2009)	*L plantarum*	*L plantarum* may help to disrupt the plasma membrane of *E coli* and help because a cytotoxic activity on promyelocytic leukemia cells as shown in an in vitro study.	Jarrow Formulas Ideal Bowel Support, 10 Billion Organisms V-Capsules Probiotic Supplement (GoodBelly) Probiotic GX (Nature's Bounty) Probiota Digestion Support and Critical Care (Kyolic) Probiotic Balance (Sundown Naturals) Heart Healthy Probiotic Solutions (Dr Sinatra) Digestive Health Probiotic (Nature Made)	King's Asian Gourmet Kimchi; Seoul Kimchi (Lucky Foods) PureLiving pickled beets; Wildbrine pickled beets; Wildbrine pickled ginger; Bubbies sauerkraut; Farmhouse culture sauerkraut; PureLiving sauerkraut; Wildbrine sauerkraut; Wildbrine fermented juice; Kimchi Live Shots; green and Spanish olives in glass jars; Wildbrine salsa; Kevita kombucha cleansing probiotic drink and sparkling probiotic drink; Next Foods GoodBelly by the Glass, GoodBelly Gluten Free by the Glass, Good Belly Plus Shot, GoodBelly Straight Shot and GoodBelly Supershot
Urogenital				
Motevaseli et al[17] (2013)	*L gasseri* and *L crispatus*	Study demonstrated that common vaginal *Lactobacilli* exert cytotoxic effects on cervical tumor cells, but not on normal cells, and that this cytotoxicity is independent of pH and lactate.	***L gasseri*:** Kyo-Dophilus 9 Probiotic Formula for Intestinal Balance and Immune Support Swanson *Lactobacillus gasseri* 3 Billion CFU PurFem Probiotic WITH APPLICATOR 10 Vaginal Suppositories *L crispatus* Physioflor 2 Vaginal Tablets	None
Cribby et al[15] (2008)	*Lactobacillus* strains *L acidophilus*	In vitro studies have shown that *Lactobacillus* strains can disrupt BV and yeast biofilms and inhibit the growth of urogenital pathogens In a study of 120 children with persistent primary vesicoureteral reflux, *L acidophilus* treatment daily was as effective as trimethoprim/sulfamethoxazole in reducing the rate of a urinary tract infection.	*L* spp including *L plantarum* and FOS, Synbiotic 2000, Mega Foods (Mega Flora) *L Reuteri* Plus with *L rhamnosus*, *L acidophilus*, & FOS (Swanson) NOW Foods BerryDophilus (chewables) Ther-Biotic Complete (Klaire Labs)	Fermented vegetables, such as fermented cabbage and other vegetables found in Korean kimchi, sauerkraut and pickled vegetables. Kefir, yogurt and buttermilk. Yogurt, milk and other dairy products enriched with live acidophilus cultures plant sources, such as whole-wheat foods, barley, onions, tomatoes, bananas and garlic. Honey also contains varying concentrations of acidophilus. Almond Dream nondairy yogurt; Amande cultured almond milk; Kite Hill almond milk yogurt; Coconut Grove organic cultured coconut milk; Nancy's Organic cultured soy; Stonyfield Organic O'Soy soy yogurt; Dahlicious cow's milk lassi; Nancy's Organic yogurts; Wallaby Yogurt Company organic Greek whole milk plain yogurt; Redwood Hill farm goat milk yogurt; Bellwether Farms sheep's milk yogurt; Green Valley Organics lactose-free kefir; Nancy's Organic low-fat plain kefir; Redwood Farm goat milk kefir.

Table 1. (continued)

Cancer	Strains	Overview	Professional and Commercial Supplements	Foods
Breast				
Aragón et al[12] (2014)	*L reuteri* ATCC-PTA-6475 *L casei* CRL-431	Inhibition of mammary neoplasia -LAB triggered $CD4^+CD25^+$ lymphocytes that convey transplantable anticancer protection. Decrease of tumor growth in mice fed preventively with LAB and also in mice fed probiotic after tumor detection.	Everidis Health Sciences - BioGaia Gastrus - 30 Chewable Tablets (*L reuteri* ATCC-PTA-6475) *L casei* CRL 431 (not commercially available)	Fermented milks; soy milk; Zukay Live Foods Veggie Kvass, Fruit Kvass; Almond Dream nondairy yogurt; Amande cultured almond milk; Nancy's Organic cultured soy; Dahlicious cow's milk lassi; DanActive; Green Valley Organics lactose-free kefir; Nancy's Organic low-fat plain kefir; Redwood Hill Farm goat milk kefir
Aragón et al[12] (2014)	*L plantarum* strain enriched with selenium nanoparticles	Tumor volumes of mice treated with selenium nanoparticle-enriched probiotic were decreased and their survival rate increased compared to mice that received probiotic alone or control mice in 4T1 breast cancer bearing mice.	Synbiotic 200 (*L* spp including *L plantarum* and FOS) Mega Foods Mega Flora (*L* spp including *L plantarum*) ***L plantarum*:** Jarrow Formulas Ideal Bowel Support, 10 Billion Organisms V-Capsules Probiotic Supplement (GoodBelly) Probiotic GX (Nature's Bounty) Probiota Digestion Support and Critical Carev (Kyolic) Probiotic Balance (Sundown Naturals) Heart Healthy Probiotic Solutions (Dr Sinatra) Digestive Health Probiotic (Nature Made)	***L plantarum*:** Fermented vegetables, Kevita probiotic drinks, olives (green), pickled vegetables, fermented salsa. (Not indicated for HIV/AIDS) NextFoods GoodBelly By the Glass, GoodBelly Gluten Free By the Glass, Good Belly Plus Shot, GoodBelly Straight Shot, GoodBelly Supershot
Aragón et al[12] (2014)	*L casei* spp *casei* ATCC-39392	Decrease of tumor growth rate and prolongation of mice survival in mice bearing invasive ductal carcinoma.	Isolated for research purposes only.	None
Aragón et al[12] (2014)	*L acidophilus* (isolated from traditional home-made yogurt and from neonatal stool)	Significant decrease of tumor growth in 4T1 tumor bearing mice due to modulation of the host's immune response.	Synbiotic 2000 Mega Flora (Mega Foods) Symbiotic 2000 *L reuteri* Plus with *L rhamnosus*, *L acidophilus*, & FOS (Swanson) NOW Foods BerryDophilus (chewables) Yogurt contains *L delbrueckii* var. *bulgaricus* and *S thermophilus* (commercial yogurt)	Traditional home-made yogurt, Almond dream nondairy yogurt, Amande cultured almond milk, Kite Hill almond milk yogurt, Coconut Grove organic cultured coconut milk, Nancy's Organic cultured soy, Stonyfield Organic O'Soy soy yogurt, Dahlicious cow's milk lassi, Nancy's Organic yogurts, Wallaby Yogurt Company organic Greek whole milk plain yogurt, Redwood Hill farm goat milk yogurt, Bellwether Farms sheep's milk yogurt, Green Valley Organics lactose-free kefir, Nancy's Organic low-fat plain kefir, Redwood Farm goat milk kefir
Cervical				
Okawa et al[16] (1993)	LC9018 (a biologic response modifier prepared from heat killed *L casei* YIT9018)	LC-9018 was shown to be an effective agent for adjuvant immunotherapy when combined with radiation therapy in the treatment of stage III cervical cancer	Isolated for research purposes only.	None
Hepatocellular Carcinoma				
Danino et al[31] (2015)	Probiotic *bacterium*, *E coli* Nissle-1917, PROP-Z	Engineered to carry specific gene circuits that enable tumor detection in urine, to liver metastases. Probiotic can sensitively, specifically, and safely detect the presence of hepatic tumors in 2 models of liver metastasis. Oral delivery of PROP-Z generated a high-contrast urine signal through selective expansion of the probiotic in liver metastases.	Engineered bacterial strain-isolated for research purposes only.	None

Table 1. (continued)

Cancer	Strains	Overview	Professional and Commercial Supplements	Foods
Colorectal				
Chen et al[5] (2015)	*C butyricum* and *B subtilis*	*C butyricum* and *B subtilis* inhibited the proliferation of CRC cells, caused cell cycle arrest and promoted apoptosis. The molecular mechanism involved reduced inflammation and improved immune homeostasis. This work establishes a basis for the protective role of probiotics *B subtilis* and *C butyricum* in intestinal tumorigenesis.	AOR Probiotic-3 (*C butyricum*) Miyarisan MIYARISAN 630 Tablets (*C butyricum*)	Fermented milk and cheeses
Bazzan et al[8] (2014)	VSL#3, contains 450 billion bacteria including *S thermophilus*, *B breve*, *B longum*, *B infantis*, *L acidophilus*, *L plantarum*, *L paracasei*, and *L delbrueckii* spp *bulgaricus*	Beneficial intestinal microbiota due to their regulatory function of gut immune response can prevent or retard neoplastic growth. Probiotic bacteria can produce metabolites such as conjugated linoleic acid, a polyunsaturated fatty acid that has anticarcinogenic effects.	VSL#3 (Sigma-Tau Pharmaceuticals, Inc)	**VSL#3 specific strains:** None
Vyas et al[9] (2012)	*L rhamnosus* GG +*B lactis* Bb12 (10B each with inulin)	Polypectomized and colon cancer patients treated with probiotics revealed increased *L rhamnosus* and *B lactis* in feces, reduction in *C perfringens*, prevents increased secretion of IL-2 in polypectomized patients, increased production of interferon-γ in cancer patients.	Culturelle (*L rhamnosus* GG) Walgreens Probiotic (*Lactobacillus* GG) Advanced Multi-Billion Dophilus - Solgar (*L rhamnosus* GG) ULTRAFLORA BALANCE by Metagenics (*L acidophilus* NCFB 1748) TruBiotics - Bayer (*B lactis* Bb12)	***L rhamnosus* GG:** None *B lactis* Bb12: Nancy's Organic cow's milk kefir
Zhong et al[10] (2014)	*L acidophilus* *L reuteri* *L acidophilus* and *L rhamnosus* *L acidophilus* and *L casei* *B longum* and *L acidophilus* *S thermophiles* *L acidophilus*, LTA-deficient, *L acidophilus* *L acidophilus*, *L casei*, *B longum*, *L casei* Shirota *B adolescentis*, *LTA-de cient*, *L acidophilus*, *P pentosaceus* FP3 *L salivarius* FP25 *L salivarius* FP35 *E faecium* FP5	Anticancer cell growth and differentiation. Direct induction of Beclin-1 and GRP78 proliferation (COX-2, cyclin D1), and cell survival (BCL-2, BCL-xL) Enhances MAPK activities including c-Jun N-terminal kinase and p38 MAPK. Induce Beclin-1 and GRP78, as well as indirectly through the induction of BCL-2 and BAK 5- fluorouracil apoptosis induction. Antioxidative activity, inhibiting linoleic acid peroxidation releasing reactive oxygen species protective factors stimulate dendtritic cells to produce inflammatory cytokines IL-12, and regulatory IL-10 induces IL-10 in DCs, downregulates IL-12 levels, increases densities of effector Foxp3+RORγt-Tregs. Enhance the total numbers of T cells, natural killer cells, major histocompatibility complex II + cells, and $CD4^{-}CD8^{+}$ T cells induces cytokines, such as interferon gamma, IL-1β, and TNF-α. Increases the production of TNF-α enhances the expression of tumor suppressor genes adhere to colon cancer cells and trigger bioproduction of short-chain fatty acids.	Klaire Labs Ther-Biotic Complete (*L rhamnosus*, *L acidophilus*, *L casei*, *L plantarum*, *L salivarius*, *B longum*, *L bulgaricus*, *L paracasei*, *B lactis*, *B breve, B bifidum*) Mega Foods Mega Flora; Innate Flora 5-14 Complete Care (*B longum*)	Dairy and fermented foods; Almond Dream nondairy yogurt; Amande cultured almond milk; Kite Hill almond milk yogurt; Coconut Grove organic cultured coconut milk; Nancy's Organic cultured soy; Stonyfield Organic O'Soy soy yogurt; Dahlicious cow's milk lassi; Nancy's Organic yogurts; Wallaby Yogurt Company organic Greek whole milk plain yogurt; Redwood Hill farm goat milk yogurt; Bellwether Farms sheep's milk yogurt; Green Valley Organics lactose-free kefir; Nancy's Organic low-fat plain kefir; Redwood Farm goat milk kefir
Lee et al[4] (2015)	*L lactis* NK-34	The anti-inflammatory effect of *L lactis* NK-34 was demonstrated by decreases of NO production and proinflammatory cytokines. These results suggest that *L lactis* NK34 could be used as a probiotic microorganism for its anticancer and anti-inflammatory effects.	None	Yogurts produced in Sweden; Jeotgal (fermented fish-Korean); fermentation starter in dairy or fermented foods; Activia dairy drink; Green Valley Organics lactose-free kefir

Table 1. (continued)

Cancer	Strains	Overview	Professional and Commercial Supplements	Foods
Donaldson[5] (2004)	*L* species and *E aerofaciens*	Both producers of lactic acid, were associated with the populations with the lower risk of colon cancer.	***Lactobacillus*:** Klaire Labs Ther-Biotic Complete Synbiotic 2000™ Mega Flora (Mega Foods) *L Reuteri* Plus (Swanson) NOW Foods BerryDophilus (chewables) ***E aerofaciens*:** None	***Lactobacillus* spp:** Various cultured and fermented foods (See Tables 1 and 2) ***E aerofaciens*:** None
Haghshenas et al[11] (2015)	*L plantarum* 17C and *L plantarum* 13C	Displayed a desirable tolerance to low pH and high concentrations of bile salts, favorable anti-pathogen activity, and acceptable antibiotic susceptibility. Thus, these 2 strains can be considered as potential probiotics. In addition, *L plantarum* 17C showed significant antiproliferative effects on HT-29 human colon cancer cell line.	None	Cheese, sourdough, wine, beer, silage, fermented plants, and meat; NextFoods GoodBelly By the Glass, GoodBelly Gluten Free by the Glass, Good Belly Plus Shot, GoodBelly Straight Shot, GoodBelly Supershot
Goldin et al[7] (1996); Lidbeck et al[39] (1991)	*L acidophilus* and *Bifidobacterium* spp	Found to reduce the levels of fecal enzymes such as beta-glucuronidase, azoreductase, nitro-reductase and urease responsible for catalyzing the conversion of carcinogenic amines.	NOW BerryDophilus (kids) contains *L acidophilus* Klaire Labs Theri-Biotic Factor 4 is a *Bifidobacterium* only supplement containing *B bifidum*, *B longum*, *B lactis*, and *B breve*	Lassi, kefir, yogurt; Almond Dream nondairy yogurt; Amande cultured almond milk; Kite Hill almond milk yogurt; Coconut Grove organic cultured coconut milk; Nancy's Organic cultured soy; Stonyfield Organic O'Soy soy yogurt; Dahlicious cow's milk lassi; Nancy's Organic yogurts; Wallaby Yogurt Company organic Greek whole milk plain yogurt; Redwood Hill farm goat milk yogurt; Bellwether Farms sheep's milk yogurt; Green Valley Organics lactose-free kefir; Nancy's Organic low-fat plain kefir; Redwood Farm goat milk kefir
Goldin et al[7] (1996)	LGG; *L rhamnosus* GG (ATCC-53103)	Goldin et al[7] have reported that LGG can protect against the formation of a dimethylhydrazine-induced colon cancer in rats.	Culturelle (*L rhamnosus* GG) Walgreens Probiotic *L rhamnosus* GG Advanced Multi-Billion Dophilus – Solgar (*L rhamnosus* GG)	None
Hepatocellular Carcinoma				
Tao et al[18] (2015)	*L rhamnosus* LC-705	Probiotics may be helpful in the treatment of hepatocellular carcinoma by preventing progression by improving endotoxemia.	N/A	N/A
El-Nezami et al[19] (2006)	*L rhamnosus* LC-705 *P freudenreichii* subsp *shermanii* strains	A study by El-Nezami et al[19] showed that a probiotic supplement reduced the biological dose of aflatoxin exposure and may offer an effective dietary approach to decrease the risk of hepatocellular carcinoma.	None—most supplements use *L rhamnosus* GG, which persists in the gut longer.	Yogurt and dairy products such as fermented and unpasteurized milk and semihard cheese; Almond Dream nondairy yogurt; Amande cultured almond milk; Trader Joe's cultured coconut milk; Nancy's Organic cultured soy; Nancy's Organic yogurts; Green Valley Organics lactose-free kefir; Nancy's Organic low-fat plain kefir; Redwood Hill Farm goat milk kefir; Kevita kombucha masterbrew; Kevita kombucha sparkling probiotic drink

Table 1. (continued)

Cancer	Strains	Overview	Professional and Commercial Supplements	Foods
Lung				
Gui et al[20] (2015)	*Lactobacillus* spp	Commensal microbiota contributes to the anti-lung-cancer response and probiotics cotreatment can enhance the antigrowth and proapoptotic effects of cisplatin.	Ther-Biotic Complete (Klaire Labs) Synbiotic 2000 Mega Flora (Mega Foods) *L reuteri* Plus (Swanson) NOW Foods BerryDophilus (chewables)	Yogurt and dairy products, fermented plant foods. (See Tables 1 and 2.)
Bladder				
Donaldson[5] (2004)	*L casei*	Two trials of patients with superficial bladder cancer. In the first trial, the probiotic group had a 50% disease free time of 350 days, compared with 195 days for the control group. The second trial also showed that the probiotics worked better than the placebo, except for recurring tumors.	PerioBiotic ™ Toothpaste-Designs for Health (*L casei*) Ther-Biotic Complete (Klaire Labs) NOW Gr8 (Dophilus) Super 5 Lozenge Probiotic (Flora, Udo's Choice) Super 5 Probiotic (Udo's Choice), Flora Ultra (Jarro-Dophilus), Jarro-Dophilus + FOS (Jarrow Formulas)	Raw or fermented dairy and fresh or fermented plant products. Including yogurt, cheese, and fermented green olives; Zukay Live Foods Veggie Kvass, Fruit Kvass; Almond Dream nondairy yogurt; Amande cultured almond milk; Nancy's Organic cultured soy; Dahlicious cow's milk lassi; Nancy's Organic yogurts; Green Valley Organics lactose-free kefir; Nancy's Organic low-fat plain kefir; Redwood Hill Farm goat milk kefir
Lymphoma				
Hosoya et al[21] (2014)	*L helveticus* SBT-2171 (LH2171)	Findings suggest that LH-2171 inhibits the proliferation of lymphocytes through a suppression of the JNK signaling pathway and exerts an immunosuppressive effect in vivo.	Used for research only. Primarily used as a cheese starter.	Used in starter cultures in the manufacture of gouda-mozzarella, cheddar, Parmesan, and Swiss cheeses; certain types of fermented milk
Castro et al[23] (2010)	*E faecalis* CECT7121	Affected multiple factors of the tumor establishment by downregulating the LBC cell proliferation and inducing apoptosis in these cells; and enhancing the immune response that protects animals from lymphoma challenge and rechallenge.	None	None
Yamamoto et al[22] (2014)	*L johnsonii*	Inoculation with *L johnsonii* in Atm-/- mice decreased measures of DNA damage, oxidative stress, and inflammation. *L johnsonii* in rat intestines has been shown to have a positive effect on oxidative stress and inflammation and prolongs the development of diabetes.	Nestlé (Lausanne, Switzerland)	Milk and dairy products
Kailasapathy et al[21] (2000); McIntosh et al[40] (1996)	*L acidophilus* and *Bifidobacterium* spp	The antitumor action of probiotics may be due to (1) inhibition of carcinogens and/or procarcinogens (2) inhibition of bacteria that convert procarcinogens to carcinogens; (3) activation of the host's immune system; (4) reduction of intestinal pH to reduce microbial activity; and (5) alteration of colonic motility and transit time.	Klaire Labs Theri-Biotic Factor 4 is a *Bifidobacterium* only supplement containing *B bifidum*, *B longum*, *B lactis*, and *B breve* ***Lactobacillus*:** Ther-Biotic Complete (Klaire Labs) Synbiotic 2000 Mega Flora/Innate (Mega Foods) *L reuteri* Plus (Swanson) NOW Foods BerryDophilus (chewables)	Almond Dream nondairy yogurt; Amande cultured almond milk; Kite Hill almond milk yogurt; Coconut Grove organic cultured coconut milk; Nancy's Organic cultured soy; Stonyfield Organic O'Soy soy yogurt; Dahlicious cow's milk lassi; Nancy's Organic yogurts; Wallaby Yogurt Company organic Greek whole milk plain yogurt; Redwood Hill farm goat milk yogurt; Bellwether Farms sheep's milk yogurt; Green Valley Organics lactose-free kefir; Nancy's Organic low-fat plain kefir; Redwood Farm goat milk kefir

Abbreviations: LGG, *Lactobacillus rhamnosus* GG; IL, interleukin; TNF-α, tumor necrosis factor alpha; POS, pectic oligosaccharides; CRC, colorectal cancer; NO, nitric oxide.

Conclusion

Although the role of various probiotic species in cancer is still being defined, the research points to regulation of various factors. Kailasapathy and Chin[32] stated, "The antitumor action of probiotics may be due to: (i) inhibition of carcinogens and/or procarcinogens (ii) inhibition of bacteria that convert procarcinogens to carcinogens (iii) activation of the host's immune system; (iv) reduction of intestinal pH to reduce microbial activity; and (v) alteration of colonic motility and transit time." The omics revolution is advancing this field faster than the studies can be produced, resulting in a "wild-west" approach to treatment options. Although there are adequate studies, most do not control for every -omics variable such as genomics, epigenetics, proteomics, transcriptomics or metabolomics. In the coming years, the expected level and degree of precision medicine is expected to explode. These posits will be answered and it is expected that in addition to the microbiome and genome, there will also be other -iomes, such as the virome, proteome, and transcriptome, that help to cement our future therapy decision.

Nutritional Supplements Overview

Professional and commercial dietary supplements containing probiotics are widely available.[33] In 2002, it was estimated that more than 100 companies in the United States marketed probiotic supplements and nearly 2 million adults consume them regularly.[34] In 2012, probiotic or prebiotic use was the third most commonly used nonvitamin, nonmineral dietary supplement and global sales are projected to reach to $42 billion by the end of 2016.[35] Using probiotics for general health versus targeting a specific health concern is more complex as the properties of probiotic species are strain specific.[36] Unfortunately, research models lack consistency in naming therapeutic strains while in addition, specific strains are often not listed on supplement labels. This challenge prevents the practitioner from distinguishing the researched strain from the supplemental product and is a limitation of these tables. If the researched strain was not readily available on the label or marketing material, the brand, potentially containing the strain, was not included in the table.

The Joint Food and Agriculture Organization of the United Nations/World Health Organization Expert Consultation on Evaluation of Health and Nutritional Properties of Probiotics developed guidelines for evaluating probiotics in food. A combination of phenotypic and genotypic tests must be performed to determine the strain; however, regulations on species identification is not in place and supplement companies are not required to list this information on labels. During this multiseries review, 30 species were specifically isolated for research purposes and were unavailable and another 56 strains were not commercially available. Due to the wide variety of formulations on the market, lack of knowledge, and poor labeling, it is difficult for practitioners and consumers to determine which brand contains specific strains researched to address a particular health concern.

This table is designed to be a resource to see what is available "at-a-glance." The brands were chosen by searching the probiotic strain and/ strain-species in Google, several supplement companies, Probiotics Advisor,[37] and the Clinical Guide to Probiotic Products.[38] Based on the results and to determine what was commercially available, the search was refined using Google Shopping. In some instances, the supplement company was called to determine if the formula contained a specific species.

Table 2. Summary of Nutritional Supplements by Cancer Type

Bladder	PerioBiotic Toothpaste Designs for Health	*L casei*
Bladder	Ther-Biotic Complete (Klaire Labs)	*L casei*
Bladder	NOW Gr8 (Dophilus)	*L casei*
Bladder	Flora, Super 5 Lozenge Probiotic (Udo's Choice)	*L casei*
Bladder	Ultra Jarrow (Dophilus)	*L casei*
Breast	BioGaia Gastrus - 30 Chewable Tablets (Everidis Health Sciences)	*L reuteri* ATCC-PTA-6475
Breast	Isolated for research purposes	*L casei sbsp casei* ATCC 39392
Breast	Not Available	*L casei* CRL 431
Breast	Not Available	*L plantarum* strain enriched with selenium nanoparticles
Breast	Widely Available	*L acidophilus* (isolated from traditional home-made yogurt and from neonatal stool)
Breast	Synbiotic 2000 (*Lactobacillus* spp including *L plantarum* and FOS)	*L plantarum*, *L acidophilus*
Breast	Mega Flora (Mega Foods)	*L plantarum*, *L acidophilus*
Breast	Ideal Bowel Support, 10 Billion Organisms V-Capsules (Jarrow Formulas)	*L plantarum*
Breast	Probiotic Supplement (GoodBelly)	*L plantarum*
Breast	Probiotic GX (Nature's Bounty)	*L plantarum*
Breast	Probiota Digestion Support and Critical Care (Kyolic)	*L plantarum*
Breast	Probiotic Balance (Sundown Naturals)	*L plantarum*
Breast	Heart Healthy Probiotic (Dr Sinatra)	*L plantarum*
Breast	Digestive Health Probiotic (Nature Made)	*L plantarum*
Breast	*L Reuteri* Plus with *L rhamnosus,* Acidophilus & FOS (Swanson)	*L acidophilus*
Breast	NOW Foods BerryDophilus (chewables)	*L acidophilus*
Cervical	Isolated for research purposes only	LC9018 (a biologic response modifier prepared from heat-killed *L casei* YIT9018)
Colorectal	Advanced Multi-Billion Dophilus (Solgar)	*L rhamnosus* GG
Colorectal	AOR Probiotic-3	*C butyricum*
Colorectal	Culturelle (iHealth)	*L Rhamnosus* GG

Table 2. (continued)

Colorectal	Innate Flora 5-14 Complete Care	*B longum*
Colorectal	Ther-Biotic Complete (Klaire Labs)	*L rhamnosus*, *L acidophilus*, *L casei*, *L plantarum*, *L salivarius*, *B longum*, *L bulgaricus*, *L paracasei*, *B lactis*, *B breve*, *B bifidum*
Colorectal	Mega Flora (Mega Foods)	*B longum*
Colorectal	Miyarisan	*C butyricum*
Colorectal	Not Available	*B subtilis*
Colorectal	TruBiotics (Bayer)	*B lactis* Bb12
Colorectal	VSL#3 (Sigma-tau Pharmaceuticals, Inc)	VSL#3 - *B longum*, *B infantis*, *B breve*, *L acidophilus*, *L casei*, *L delbrueckii* subsp, *L bulgaricus*, *L plantarum*, and *Streptococcus salivarius* subsp *Thermophiles*
Colorectal	ULTRAFLORA BALANCE (Metagenics)	*L acidophilus* NCFB 1748
Colorectal	Probiotic *Lactobacillus* GG (Walgreens)	*Lactobacillus* GG
Hepatocellular Carcinoma	Not Available	*L rhamnosus* LC705
Hepatocellular Carcinoma	Probiotic bacterium *E coli* Nissle 1917, PROP-Z	Engineered bacterial strain-isolated for research purposes only
Leukemia	Chewable tablets, mandarin orange (BioGaia Gastrus)	*L reuteri* ATCC PTA 6475
Leukemia	Digestive Health Probiotic (Nature Made)	*L plantarum*
Leukemia	Garden of Life RAW for women	*Bifidobacterium* spp
Leukemia	Gr8-Dophilus NOW	*Bifidobacterium* spp
Leukemia	Heart Healthy Probiotic Solutions (Dr Sinatra)	*L plantarum*
Leukemia	Innate Flora 5-14 Complete Care	*L casei*
Leukemia	Isolated for research purposes only	*L reuteri* 100-23
Leukemia	Isolated for research purposes only	*L gasseri 311476*
Leukemia	Isolated for research purposes only	*L kefiri* P-IF
Leukemia	Ideal Bowel Support, 10 Billion Organisms V-Capsules (Jarrow Formulas)	*L plantarum*
Leukemia	Mega Flora (Mega Foods)	*L casei*
Leukemia	Mega Flora/Flora 5-14 Complete Care (Mega Foods)	*Bifidobacterium* spp
Leukemia	Not available	*Roseburia* spp
Leukemia	Not available	*Bacteroides* spp
Leukemia	Not available	*B dorei*
Leukemia	PerioBiotic Toothpaste - Designs for Health	*L casei*
Leukemia	Probiata Digestion Support and Critical Care (Kyolic)	*L plantarum*
Leukemia	Probiotic Balance (Sundown Naturals)	*L plantarum*
Leukemia	Probiotic GX (Nature's Bounty)	*L plantarum*
Leukemia	Probiotic Supplement (GoodBelly)	*L plantarum*
Leukemia	Ther-Biotic Factor 4 (*Bifidobacterium* Complex) 60c by Klaire Labs (*Bifidobacterium breve)*	*B breve*
Lung	Ther-Biotic Complete (Klaire Labs)	*Lactobacillus* spp
Lung	Synbiotic 2000	*Lactobacillus* spp
Lung	Mega Flora (Mega Foods)	*Lactobacillus* spp
Lung	*L reuteri* Plus (Swanson)	*Lactobacillus* spp, *L acidophilus*
Lung	NOW Foods BerryDophilus (chewable)	*Lactobacillus* spp, *L acidophilus*
Lung	None available	*L plantarum* 17C and *L plantarum* 13C
Lung	Symbioflor 2	*E coli*
Lymphoma	Used for research only. Primarily used as a cheese starter.	*L helveticus* SBT2171 (LH2171)
Lymphoma	None available	*E faecalis* CECT7121
Lymphoma	Nestlé (Lausanne, Switzerland)	*L johnsonii*
Lymphoma	NOW BerryDophilus (kids)	*L acidophilus* and *Bifidobacterium* spp
Lymphoma	Ther-Biotic 4 (Klaire Labs)	*Bifidobacterium* spp (*B bifidum, B longum, B lactis* and *B breve*)
Lymphoma	Mega Flora (Mega Foods)	*B longum, Bifidobacterium* spp, *L acidophilus*
Lymphoma	Innate Flora 5-14	*B longum, Bifidobacterium* spp, *L acidophilus*
Lymphoma	Complete Care	*B longum*
Lymphoma	Culturelle	*L rhamnosus* GG
Lymphoma	Probiotic *L rhamnosus* GG (Walgreens)	*L rhamnosus* GG
Lymphoma	Advanced Multi-Billion Dophilus (Solgar)	*L rhamnosus* GG
Lymphoma	Synbiotic 2000	*L acidophilus*
Urogenital	Mega Flora (Mega Foods)	*Lactobacillus* spp including *L plantarum* and FOS
Urogenital	Synbiotic 2000	*Lactobacillus* spp including *L plantarum* and FOS
Urogenital	*L Reuteri* Plus with *L rhamnosus,* Acidophilus & FOS (Swanson)	*L acidophilus*
Urogenital	NOW Foods BerryDophilus (chewables)	*L acidophilus*
Urogenital	Ther-Biotic Complete (Klaire Labs)	*L acidophilus*
Urogenital	Dophilus 9 probiotic formula for intestinal balance and immune support (Kyro)	*L gasseri*
Urogenital	*L Gasseri* 3 Billion CFU (Swanson)	*L gasseri*
Urogenital	PurFem Probiotic WITH APPLICATOR 10 vaginal suppositories	*L gasseri*
Urogenital	PhysioFlor 2 vaginal tablets	*L crispatus*

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