REVIEW ARTICLE

Probiotics and Disease: A Comprehensive Summary—Part 7, Immune Disorders

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Abstract

This article series provides a literature review of the disease-specific probiotic strains associated with immune and autoimmune conditions that have been studied in published clinical trials in 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, and the second article (part 2) explored cultured and fermented foods that are commonly available in the United States. The third article (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. The fourth article (part 4) elucidated the role of the microbiome in infectious diseases, and the fifth article (part 5) examined respiratory conditions of the ears, nose, and throat. The sixth article (part 6) explored the relationship between beneficial microbiota and skin disorders. This seventh article (part 7) reviews the relationship between beneficial microbiota and autoimmune diseases, allergies, asthma, and other immunity-related disorders. Future articles will review the relationship between probiotics and skin disorders, the influence of the microbiome on cancer development and prognosis, and gastrointestinal and genitourinary diseases associated with dysbiosis, followed by an article focused on probiotic supplements. This literature review is specific to disease condition, probiotic classification, and individual strain.

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We investigated disease-specific probiotic strains associated with autoimmune diseases such as type 1 diabetes, connective tissue disease, and myasthenia gravis. This is not an exhaustive review.

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 visiting grocery stores (primarily in California).

Understanding the Role of the Microbiome and Immune Function

Although supplementation with probiotics is extremely helpful in helping to prevent or mitigate the effects of immune disorders, the influence of diet on the microbiome should not be underestimated. Carbohydrates, proteins, fats, and fiber are essential dietary components and these macronutrient balances can be directly responsible for cell damage and the resulting inflammation that may trigger autoimmunity. Specifically, both fat and fiber intakes exert a strong influencer on the microbiome. Fiber intake is declining in Westernized societies. Higher fiber intakes not only help reduce the incidence of colon cancer, but the lack of fiber and its effects on the microbiome can also be partially responsible for the rise in allergy syndromes and autoimmunity.

Dietary fiber is consumed by various bacterial species in the microbiome, which then produce short-chain fatty acids (SCFAs; acetate, propionate, and butyrate).[1] This is important for colon health, because butyrate is the primary fuel for the colonocyte. Decreased production of SCFAs is highly correlated with intestinal permeability, which, in turn, leads to the destruction of immune tolerance and intestinal inflammation associated with diseases including celiac disease, colorectal cancer, allergies, asthma, chronic kidney diseases, and type 1 diabetes.[1] On the contrary, diets high in fiber generate ample SCFAs exerting anti-inflammatory and immunomodulatory effects via T-regulatory (Treg) cell generation. Tregs are responsible for actively inhibiting the immune system from overreaction during infections while also playing an important role in the prevention of autoimmune disease via self-recognition.[2] According to Smigiel,[2] "Excessive Treg activity can lead to immunodeficiency, chronic infection and cancer, (while) too little Treg activity results in autoimmunity and immunopathology, and impairs the quality of pathogen-specific responses." Once bacteria have positively influenced the production of Treg cells, this helps to tip the cytokine production in the favor of anti-inflammatory cytokines such as interleukin (IL) 10.[2,3]

The specific bacterial species present in the microbiome are also strong influencers of the immune response. There are several species such as *Lactobacillus plantarum* CCFM47, *Lactobacillus acidophilus* CCFM137, *Lactobacillus casei* LC2, *Lactobacillus rhamnosus* GG, *Bifidobacterium lactis*, *Lactobacillus casei* DN-114001, *Lactobacillus salivarius*, and *Lactobacillus reuteri* ATCC23272,[4,5] which stimulate the immune system to produce Treg cells, which is important in regulating the T-helper 1/T-helper 2 (T_h1/T_h2) balance:

> T-helper 1 (T_h1) cells produce interferon (IFN)-gamma, IL-2 and tumor necrosis factor (TNF)-beta, (and) evoke cell-mediated immunity and phagocyte-dependent inflammation. T_h2 cells, which produce IL-4, IL-5, IL-6, IL-9, IL-10, and IL-13, evoke strong antibody responses (including those of the IgE class) and eosinophil accumulation, but inhibit several functions of phagocytic cells (phagocyte-independent inflammation).[6]

These species, in the form of probiotics, also confer increased induction of tolerogenic antigen-presenting cells, which then generate Tregs. In this way, bacterial diversity has the potential to favorably regulate inflammatory diseases such as autoimmunity and allergies. In some cases, these bacterial species produce more potent Treg cells than were found before exposure to probiotics. Specifically, *L reuteri* was found to help prevent allergic inflammation of the airways. The influence exerted on Tregs by bacteria also affect nuclear factor kappa beta (NF-kB). *L plantarum*, for example, helps to stop NF-kB from breakdown by blocking proteasome function. Conversely, *Bifidobacterium infantis* appears to decrease NF-kB activation while increasing the amount of FOXP4 cells in both the mucosa and spleen. FOXP4 cells are responsible for cell type-specific gene transcription, and alterations in its function can increase the risk for certain cancers. This increase helps to provide protection against pathogenic species and favorable self-immunity.[7]

This positive influence of fiber on the immune system does not stop in the gut, as diet-derived microbial metabolites move across the mucosa to the lamina propria and then into systemic circulation via the portal vein. Although butyrate is primarily found in the colon, acetate is easily detectable in the periphery and appears to regulate the immune system both in and out of the gut.[1] In this way, SCFAs may protect against the development of autoimmune diseases. Even in utero, SCFAs pass through the placenta from the mother to the child, which may

protect against inflammatory asthma via epigenetic influence. This is the result of gene transcription, specifically FOXP3 target genes, which are essential for tolerance/autoimmunity. FOXP3, like FOXP4, is important for Treg development and function and the 3 isoform is considered to be the master regulatory enzyme. It does so by generating Tregs and upregulating their function within the colon. FOXP3 is also responsible for exerting epigenetic effects required for extrathymic generation of Tregs.[1]

Table 1. Selected Immune Conditions

Immune Conditions	Strains	Overview	Professional and Commercial Products	Foods
Type 1 Diabetes				
Kingma et al[27] (2011)	*L johnsonii* N62	*L johnsonii* N62 reduced the rate of type 1 diabetes in BioBreeding diabetes-prone rats by decreasing proinflammatory cytokines, IFN-γ, and TNF-α. This probiotic activates the innate immune response via an increased expression of CCL20 (MIP3A), CXCL8 (IL-8), and CXCL10 (IP10).	*L johnsonii* N62 isolated from BB-DR rats for research purposes and not available commercially.	***L johnsonii* N62:** None identified.
Davis-Richardson et al[8] (2015)	*Lactobacillus* and *Firmicutes*	There is a significant difference in the microbiome of healthy children with genetic predisposition to type 1 diabetes than in those who have type 1 diabetes. Healthy children have high levels of *Lactobacillus* and *Firmicutes*, whereas unhealthy children have higher levels of *Bacteroides.*	*Lactobacillus* found in most commercially available probiotic supplements.	*Lactobacillus* commonly found in fermented foods and beverages.
Calcinaro et al[28] (2005)	VSL#3 (*B longum, B infantis, B breve, L acidophilus, L casei, L delbrueckii* subsp, *L bulgaricus, L plantarum*, and *S salivarius* subsp Thermophilus)	VSL#3 helped prevent diabetes development in NOD mice with decreased insulitis and rate of b-cell destruction via an increased in IL-10. In mice and humans, GALT is involved in islet-specific autoimmunity in diabetes-prone individuals. VSL#3 administration in mice works to induce IL-10-producing cells in GALT.	**VSL#3:** Sigma-tau Pharmaceuticals, Inc (*B longum*, *B infantis*, *B breve*, *L acidophilus*, *L casei*, *L delbrueckii* subsp, *L bulgaricus*, *L plantarum*, and *S salivarius* subsp Thermophiles) Sibiotica (Apex Energetics)	**VSL#3:** None
Uusitalo et al[9] (2016)	*Lactobacillus* and *Bifidobacterium* species	In children with the DR3/4 genotype, early supplementation with probiotics from the ages of 0 to 27 d decreased the risk of type 1 diabetes compared with use of probiotics after 27 d or no probiotics at all. Typical probiotic supplements used by study participants included mixtures of various *Lactobacillus* and *Bifidobacterium* species. The lack of protection provided in infants after 27 d of life may be linked to the influence of diet on the microbiome. Antibiotic use was positively associated with type 1 diabetes development.	*Lactobacillus* and bifidobacteria found in most commercially available probiotic supplements.	Cultured dairy and dairy alternatives; fermented vegetables.
Dolpady et al[29] (2016)	*Lactobacillus* species	VSL#3 with and without retinoic acid decreases risk for type 1 diabetes in NOD mice by influencing both the gut and immune system. This occurs by increasing levels of *Lactobacillus* species and improving various protolerogenic species such as *Clostridia* species in the Firmicutes phylum, which induce FOXP3+ Treg cell differentiation.	*Lactobacillus* found in most commercially available probiotic supplements.	Cultured dairy and dairy alternatives; fermented vegetables.
Kverka et al[30] (2012)	*L johnsonii*	Lactobacteria appear to be good candidates for protecting against type 1 diabetes. *L johnsonii* appears to inhibit disease development by immunomodulation, changes in the metabolism of eicosanoids, and improvement of the function of the gut barrier.	*L johnsonii* N62 isolated from BB-DR rats for research purposes and not available commercially.	***L johnsonii* N62:** None identified.
Ljungberg et al[10] (2006)	*L rhamnosus* GG, *L rhamnosus*, *B breve* BBI99, *P freudenreichii* subsp Shermanii	In a pilot study to the PRODIA Study, infants who were genetically at risk for type 1 diabetes were given a mixture of *L rhamnosus* GG (5×10^9 CFU), *L rhamnosus* LC705 (5×10^9 CFU), *B breve* BBI99 (2×10^8 CFU), and *P freudenreichii* subsp Shermanii (2×10^9 CFU). The study found that the use of these probiotics was safe and feasible but did not significantly change prevalence of autoantibodies.	***L rhamnosus* GG:** Walgreens Probiotic *Lactobacillus* GG Advanced Multi-Billion Dophilus (Solgar)	None
Systemic Lupus Erythematosus				
Lopez et al[11] (2015)	*B bifidum* LMG13195 (Bb), *R obeum* DSM25238, *B coccoides* DSM935, *Synergistetes*	Decreased *Firmicutes* to *Bacteroidetes* ratio. In SLE, IFN-γ (T_h1 cytokine) levels were negatively associated with *Bacteroidetes* and positively associated with *Firmicutes* and the *Firmicutes*:*Bacteroidetes* ratio. *Bifidobacterium* and *Clostridium* spp help to induce Treg cells, which help to balance the immune system. *B bifidum* LMG13195 (Bb) helps induce FOXP3 expression. *R obeum* DSM25238 and *B coccoides* DSM935 help induce Treg cells. *Synergistetes* were correlated in SLE with serum levels of proinflammatory and T_h17-promoting cytokine IL-6, which is associated with a humoral immune response. May also promote IgM antibodies, which could be decreased in SLE.	***B bifidum* LMG13195 (Bb):** Cultured for research purposes. ***Robeum* DSM25238 & *B coccoides* DSM935:** Not available.	None
Richards et al[1] (2016)		"In a mouse model of lupus, treatment with butyrate and synthetic HDAC inhibitors led to the suppression of mechanisms that promote hypermutated antibody responses and class-switching, which culminate in the generation of high-affinity autoantibodies."		
Allergy				
Kobayashi et al[14] (2010)	*L casei* Shirota DN-114 001 and YIT9029	*L casei* Shirota helps to improve cellular immunity by modulating the T_h1/T_h2 balance toward T_h1, improving the allergic response.	***L casei* Shirota DN-114 001 and YIT9029:** Not available.	***L casei* Shirota:** Yakult

Table 1. (continued)

Immune Conditions	Strains	Overview	Professional and Commercial Products	Foods
Issazadeh-Navikas et al[5] (2012)	*L rhamnosus* GG (ATCC53103), *B lactis* (BB-12), *L salivarius*, *L reuteri* (ATCC23272), *L casei* DN-114001	*L rhamnosus* GG (ATCC53103) and *B lactis* (BB-12) increase FOXP3 and consequently Treg cells, allowing for decreased airway reactivity in ovalbumin-induced asthma models. *L salivarius* and *L reuteri* (ATCC23272) increase FOXP3 and, therefore, Treg cells by decreasing airway reactivity in ovalbumin-induced asthma models. Improved FOXP3 levels and Treg cells and decreased delayed-type hypersensitivity by causing an increase in IL-10 in ovalbumin and 2-4-dinitroflurobenzene-sensitized mice.	***L rhamnosus* GG (ATCC 53103), JB-1:** Not available. ***B lactis* (BB-12):** One-A-Day TruBiotics (Bayer) ProSynbiotic (Standard Process) Advanced Acidophilus Plus (Solgar) ***L reuteri* (ATCC23272):** Not available. ***L salivarius*:** Gr8-Dophilus (NOW Foods) Dr. Formulated Probiotics and Primal Defense (Garden of Life) UltraFlora Spectrum (Metagenics) Flora products (Innate Response) Ultra-Strength Probiotic 10 (Nature's Bounty)	***L rhamnosus* GG (ATCC 53103), JB-1:** None ***B lactis* (BB-12):** Nancy's Organic Low-fat Kefir ***L salivarius*:** None ***L reuteri* (ATCC 23272):** None ***L casei*:** Kefir, kvass, lassi, yogurt
Vaarala[31] (2003)	Lactobacilli, enterococci, bifidobacteria, *Lactobacillus* GG, *B lactis* BB-12, *L reuteri* DSM122460, *L rhamnosus* 19070-2	Increased levels of *Lactobacilli* are more commonly found in the microbiome of infants in Estonia than those in Sweden, providing protection against allergy. Decreased levels of *Enterococci* and *Bifidobacteria* are found in the first year of life in children who developed allergies while they had higher levels of *Clostridia* and staphylococci. Decreased *Bifidobacterium* levels and increased *Clostridia* levels were found in Finnish children with atopic sensitization. Oral probiotics used in infancy may help prevent food allergies by affecting T cells in Peyer's patches. This is particularly influenced by Gram-positive or Gram-negative bacteria, including bifidobacteria or *E coli*. *Lactobacillus* GG was used in a study on children at risk for atopic disease and was given in capsules to mothers for the 2 to 4 wk before delivery and after delivery to either the breastfeeding mother or the child for 6 mo. The frequency of atopic eczema in the probiotic group was found to be half that of the placebo group. Both *B lactis* BB-12 and *Lactobacillus* GG decreased the number of infants with atopic eczema in comparison with infants given hydrolyzed formula and no probiotics. *L reuteri* DSM122460 and *L rhamnosus* 19070-2 helped to decrease eczema in children aged 1 to 13 y and decreased eosinophil cationic protein levels.	***B lactis* Bb-12:** One-A-Day TruBiotics (Bayer) ProSynbiotic (Standard Process) Advanced Acidophilus Plus (Solgar) ***L reuteri* DSM-122460:** Not available. ***L rhamnosus* 19070-2, LC705:** Not available.	***B lactis* (BB-12):** Nancy's Organic Low-fat Kefir ***L reuteri* DSM 122460, *L rhamnosus* 19070-2, LC705:** None
Furchiaroni et al[32] (2013)	Lactobacilli, bifidobacteria	Decreased amounts of both lactobacilli and bifidobacteria are closely associated with allergies.	*Lactobacillus* found in most commercially available probiotic supplements.	Cultured dairy and dairy alternatives; fermented vegetables.
Jeongmin et al[33] (2013)	*L acidophilus*, *L bulgaricus*, *B bifidum*, *B longum*, *L casei* YIT9029, *L casei* HY7201, *L brevis* HY7401, *L plantarum* HY20301	*L acidophilus*, *L bulgaricus*, *B bifidum*, and *B longum* help promote cellular immune responses by activating T_h1 cells helping to reduce total or OVA-specific IgE production as well as changing cytokine patterns in a strain-dependent manner. Mice given *L casei* YIT9029, *L casei* HY7201, *L brevis* HY7401, or *L plantarum* HY20301 every 2 d for 3 wk had decreased total IgE levels and OVA-specific IgE levels. *L casei* HY7201 induced an allergic response, whereas *L casei* YIT9029 induced higher T_h1 cytokines with a decrease in T_h2 cytokines, thus decreasing the allergic response.	***L acidophilus*, *L bulgaricus*, *B bifidum*, and *B longum*:** Combined in ImmuProbio (Health Aid) Strengtia (Apex Energetics) ***B longum*:** Mega Flora; Innate Flora 50-14 Complete Care (Mega Foods) ***L plantarum* HY20301:** Not available. ***L brevis* HY7401:** Not available.	***L acidophilus*:** Kefir, lassi, yogurt ***L bulgaricus, B bifidum*:** Kefir, all yogurt containing "live and active cultures" ***B longum, L brevis* HY7401, *L plantarum* HY20301, *L salivarius* LS01:** None ***L bulgaricus, S thermophilus*:** Kefir, all yogurt containing "live and active cultures"
Castellazzi et al[34] (2013)	*L rhamnosus*, *L casei*, *L salivarius* LS01	*L rhamnosus* used in children with atopic dermatitis decreased dermatitis, as well as TNF-α and a1-AT in feces. *L casei* DN-114001 helped to reduce by 33% the occurrence of yearly rhinitis. *L salivarius* LS01 decreased skin manifestations after 16 wk in adult atopic patients with a reduced level of *Staphylococcus* in feces and improvements in the T_h1/T_h2 cytokine profile.	***L rhamnosus*:** Walgreens Probiotic *Lactobacillus* GG Advanced Multi-Billion Dophilus (Solgar) ***L salivarius* LS01:** Not available. ***L salivarius*:** Gr8-Dophilus (NOW Foods) Dr. Formulated Probiotics and Primal Defense (Garden of Life) UltraFlora Spectrum (Metagenics) Flora products (Innate Response) Ultra-Strength Probiotic 10 (Nature's Bounty)	***L rhamnosus* GG (ATCC 53103), JB-1:** None ***L casei*:** Kefir, kvass, lassi, yogurt ***L salivarius*:** None

Table 1. (continued)

Immune Conditions	Strains	Overview	Professional and Commercial Products	Foods
Das et al[35] (2013)	*L rhamnosus* JB-1, *L gasseri* A5, *B longum* BB536, *L paracasei*, *L casei* Shirota, *L bulgaricus*, *S thermophilus*	*L bulgaricus*, *S thermophilus*, and *L casei* supplemented at 100 mL/d for 12 mo decreased episodes of asthma and rhinitis. Four capsules/day for 5.5 mo of *L rhamnosus* decreased total symptoms scores in allergic nose, eye, and lung symptoms. *L casei* Shirota provided at 80 mL/d for 8 wk changed the symptom medication score in children with allergies. *L paracasei* given at 2 capsules/day for 30 d decreased rhino-conjunctivitis in children and improved the quality of life score. *B longum* BB536 at 200 g/d 14 wk decreased subjective symptoms score in allergic adults. *L gasseri* A5 capsule provided to 105 children aged 6 to 12 y with asthma improved peak expiratory flow rates, symptoms of asthma, and allergy relief scores of the patients, as well as immunological parameters. *L rhamnosus* JB-1 provides significant inhibition of mast cell degranulation to a range of stimuli (ie, IgE-mediated activation) in rat models. Therefore, this strain may be effective as a mast cell stabilizer. In fact, this strain can downregulate FCER1 expression on mast cells.	***L rhamnosus* GG (ATCC 53103), JB-1:** Not available. ***L gasseri*:** Kyo-Dophilus 9 Probiotic Formula for Intestinal Balance and Immune Support *L Gasseri* 3 Billion CFU (Swanson) PurFem Probiotic WITH APPLICATOR 10 Vaginal Suppositories ***B longum* BB536:** Bifilon (Quality of Life Herbs) Bifido GI Balance (Life Extension) Jarro-Dophilus EPS and Baby's Jarro-Dophilus+FOS Powder (Jarrow Formulas) Tribif (Valeas) ***S thermophilus* and *L paracasei*:** BioDoph-7 Plus (Biotics Research) ***S thermophilus*:** SymBiotics with FOS Description (Nutricology)	***L rhamnosus* GG (ATCC 53103), JB-1:** None ***L bulgaricus*, *S thermophilus*:** Kefir, all yogurt containing "live and active cultures" ***L paracasei*:** Kevita Probiotic Drinks ***B longum* BB536, *L gasseri*, *B fragilis*:** None
Hendaus et al[36] (2016)	*Bifidobacterium* spp, *B fragilis*, *Lactobacillus* GG, *B lactis*, *L plantarum*, *L reuteri*, *L gasseri*, *B longum*	Whereas in breastfed infants *Bifidobacterium* spp predominate the microbiome (60% to 70%), formula-fed infants had more *Bacteroides* and *Clostridium* spp. This may lead to an increased risk of allergies and other diseases. *B fragilis* given to germ-free mice helped improve T_h1 response and balanced T_h1/T_h2. In a murine model, *Lactobacillus* GG decreased allergic airway response and peribronchial inflammation in mouse offspring. *Lactobacillus* GG or *B lactis* BB12 in a murine model decreased pulmonary eosinophilia, airway reactivity, and antigen-specific IgE production. The addition of *L plantarum* helped decrease airway eosinophilia following aerosolized allergen exposure. Giving *L plantarum* and *L lactis* helped to reduce allergen-induced basophil degranulation upon exposure to birch pollen. *L reuteri* decreased allergy response to methacholine, airway eosinophilia, and local response of cytokines. *Lactobacillus* GG may be helpful in infant eczema and dermatitis symptoms in IgE-sensitized infants, but not in non-IgE-sensitized infants. Use of yogurt containing *L gasseri*, *Lactobacillus* GG, and *B longum* may help with nasal blockage in seasonal allergic rhinitis.	***B fragilis*:** Not available. ***B longum*:** Mega Flora; Innate Flora 50-14 Complete Care (Mega Foods) ***L lactis*:** Goat Milk Kefir (Activia)	***B longum* BB536, *L gasseri*, *B fragilis*:** None
Magerl et al[37] (2008)	*E coli* (nonpathogenic)	In a murine model, colonization with very high doses of live, unfimbriated, nonpathogenic *E coli* bacteria strongly reduced mast cell degranulation.	***E coli*:** Mutaflor (Tribute Pharmaceuticals); contains the Nissle 1917 strain	None
Oksaharju et al[16] (2011)	*Lactobacillus* GG, *L rhamnosus* LC705	*Lactobacillus* GG and *L rhamnosus* LC705 suppressed genes encoding FCER1A and FCER1G, which encode allergy-related high-affinity IgE receptor subunits α and γ, respectively, and also suppressed the histamine H_4 receptor. They worked by decreasing proinflammatory mediators such as IL-8 and TNF-α, while upregulating the anti-inflammatory IL-10.	***Lactobacillus* GG:** Walgreens Probiotic Lactobacillus GG Advanced Multi-Billion Dophilus (Solgar)	None
Schiffer et al[17] (2011)	*L casei* DN-114-001	*L casei* DN-114-001 provided protection from IgE- and IgG-induced mouse mast cell activation and ex vivo on IgE-dependent human basophil activation. It appears that this strain can inhibit mast cell degranulation and the secretion of IL-5, IL-6, IL-13, TNF-α, MCP-1, and MIP-1α. These are the 4 cytokines and 2 chemokines that induce FCER1 aggregation. Further, *L casei* inhibited β-hexosaminidase release via IgG immune complexes.	***L casei* DN-114001:** Not available.	None
Forsythe et al[38] (2012)	*Lactobacillus* GG	*Lactobacillus* GG may be effective as a mast cell stabilizer. In fact, this strain is able to down regulate FCER1 (IgE receptor) expression on mast cells.	***Lactobacillus* GG:** Walgreens Probiotic *Lactobacillus* GG Advanced Multi-Billion Dophilus (Solgar)	None

Table 1. (continued)

Immune Conditions	Strains	Overview	Professional and Commercial Products	Foods
Zhang et al[39] (2016)	*L salivarius*, *L paracasei*, *B animalis*, *B bifidum*, *L rhamnosus*, *L rhamnosus* GG, *B longum*, *B lactis*, *L acidophilus*, *L lactis*, *L reuteri*, *L paracasei*	In a systematic review and meta-analysis, it was found that pre- and postnatal administration of probiotics could reduce the risk of atopy and food hypersensitivity. The mechanism is thought to be a shift of immune balance toward a T_h1 response and therefore decreased production of T_h12 cytokines such as IL-4, IL-5, and IL-13. In addition, there is decreased IgE and increased production of C-reactive protein and IgA. Probiotics protective against atopy include *L salivarius*, *L paracasei*, *B animalis*, *B bifidum*, *L rhamnosus*, *L rhamnosus* GG, *B longum*, *B lactis*, *L acidophilus*, *L lactis*, *L reuteri*, and *L paracasei.* Probiotics protective against food sensitization include *L rhamnosus*, *B animalis*, *L rhamnosus* GG, *B bifidum*, *B lactis*, *L acidophilus*, *L lactis*, and *L reuteri.*	***L salivarius*:** Gr8-Dophilus (NOW Foods) Dr. Formulated Probiotics and Primal Defense (Garden of Life) UltraFlora Spectrum (Metagenics) Flora products (Innate Response) Ultra-Strength Probiotic 10 (Nature's Bounty) ***B longum*:** Mega Flora; Innate Flora 50-14 Complete Care (Mega Foods) ***L acidophilus*, *L bulgaricus*, *B bifidum*, and *B longum*:** Combined in ImmuProbio (Health Aid) Strengtia (Apex Energetics) ***L lactis*:** RAW Probiotics Women 85 Billion CFU (Garden of Life) Perfect Biotics (Probiotic America) Jarr-Dophilus EPS 25 Billion (Jarrow Formulas) ***S thermophilus* and *L paracasei*:** BioDoph-7 Plus (Biotics Research)	***L paracasei*:** Kevita Probiotic Drinks ***L rhamnosus* GG:** None
Zajac et al[40] (2015)	*L paracasei* 33	*L paracasei* 33 helps protect against grass pollen allergy.	None	***L paracasei* 33:** None
Johansson et al[41] (2011)	*Bifidobacterium*	For children with parents who have allergies, there are lower levels of endotoxin in house dust, which decrease infant exposure to bifidobacteria species. *S aureus* was found more frequently in children with allergies.	**Bifidobacteria:** Klaire Factor 4	Cultured dairy and dairy alternatives; fermented vegetables.
Randazzo et al[18] (2014)	*L reuteri* DSM17938	*L reuteri* DSM-17938 was found to help improve both clinical symptoms and microbiome diversity in patients with SNAS.	***L reuteri* DSM-17938:** BioGaia (Gastrus)	
Kuitunen et al[19] (2009)	Probiotic mix including 2 lactobacilli, bifidobacteria, and propionibacteria	A probiotic mixture given to pregnant mothers during their final month of pregnancy and to infants during their first 6 m along with the prebiotic galactooligosaccharide, was found to prevent IgE-associated allergy until the age of 5 y, but only in children delivered by cesarean section.	Various	Cultured dairy and dairy alternatives; fermented vegetables.
Rheumatoid Arthritis				
Vitetta et al[12] (2013)	Bifidobacteria, *B fragilis*, *L casei*, *B coagulans* GBI-30, 6086, *L rhamnosus* GR-1, *L reuteri* RC-14	Compared with individuals without RA, RA patients have significantly less bifidobacteria, bacteria from the *Bacteroides-Porphyromonas-Prevotella* group, *B fragilis* subgroup, and *E rectal-C coccoides* group. Bacteria normally found in the oral cavity, including *P gingivalis* and *P intermedia*, is found in the synovial fluid of patients with RA. Antigen-specific antibodies are also found against *P gingivalis*, *P intermedia*, and *B forsythus* in these patients. *L casei* was shown to prevent RA progression in rat models by suppressing collagen-induced arthritis, decreasing paw swelling, decreased lymphocyte infiltration, and reduced destruction of cartilage. It works by decreasing proinflammatory cytokines and upregulating IL-10 levels and suppressing the T_h1 immune response that causes RA. "Compared with placebo, *Bacillus coagulans* GBI-30, 6086 treatment resulted in greater improvement in patient global assessment and self-assessed disability; reduction in CRP; as well as the ability to walk 2 miles, reach, and participate in daily activities." *L rhamnosus* GR-1 and *L reuteri* R-14 helped to functionally improve those with RA in a double-blind RCT of 29 RA patients.	**Bifidobacteria:** Klaire Factor 4 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*) ***L rhamnosus* GR-1, *L reuteri* RC-14:** UltraFlora Women's (Metagenics) Women's Fem Dophilus (Jarrow Formulas)	**Bifidobacteria:** Cultured dairy and dairy alternatives; fermented vegetables. ***B fragilis*:** None ***L casei*:** Kefir, kvass, lassi, yogurt ***B coagulans* GBI-30, 6086, *L rhamnosus* GR-1, *L reuteri* RC-14, *Lactobacillus* GG, *L fermentum*:** None
Mandel et al[13] (2010)	*B coagulans*, *Lactobacillus* GG, *L casei*	*B coagulans* showed borderline statistical significance in a double-blind RCT of 45 patients with RA in decreasing pain when included in a protocol that also included green tea extract; MSM; vitamins A, B, C, D, E and folic acid; and selenium. *Lactobacillus* GG decreased inflammation in rats as compared with rats fed yogurt. *L casei* in a 12-wk study decreased signs of arthritis, infiltration of lymphocytes into the joint, and cartilage breakdown in a rat model. Decreased levels of proinflammatory cytokines and decreased T-cell proliferation was found in combination with increased levels of the anti-inflammatory IL-10.	***Lactobacillus* GG:** Walgreens Probiotic *Lactobacillus* GG Advanced Multi-Billion Dophilus (Solgar) 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*)	***B coagulans*:** None ***Lactobacillus* GG:** None ***L casei*:** Kefir, kvass, lassi, yogurt

Table 1. (continued)

Immune Conditions	Strains	Overview	Professional and Commercial Products	Foods
Scofield[42] (2014)		Oral bacteria may be implicated in the pathogenesis of RA via molecular mimicry. In particular, *P gingivalis* may be the culprit because it is the only bacterium that contains the enzyme peptidylarginine deiminase used to convert arginine to citrulline allowing for generation of antibodies to binding citrullinated peptides in RA.		
Kwon et al[43] (2010)	*L casei*, *L acidophilus*, IRT5 probiotic (*L acidophilus*, *L casei*, *B bifidum*, *L reuteri*, and *S thermophiles*)	*L casei* decreases the proinflammatory responses via an increase in levels of IL-10. *L acidophilus* increases T_h1 cytokines. IRT5 helps to decrease autoimmunity via increasing the level of CD4+FOXP3+Tregs.	**IRT5 probiotics:** Mega Flora Plus (Mega Food) Flora 50-14 and Flora 20-14 (Innate Response) 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*) Strengtia (Apex Energetics; (*L acidophilus*, *B coagulans*)	***L casei*:** Kefir, kvass, lassi, yogurt ***L acidophilus*:** Kefir, lassi, yogurt **RT5 probiotic:** Similar to many mixtures used in kefir and yogurts.
Vaghef-Mehrabany et al[44] (2014)	*L casei* 01	*L casei* 01 significantly reduced disease activity in patients with RA helping to decrease TNF-α, IL-6, and IL-12. It also increased the anti-inflammatory IL-10.	***L casei* 01:** None.	***L casei* 01:** None
Myasthenia Gravis				
Chae et al[45] (2012)	IRT5 probiotics (*S thermophiles*, *L reuteri*, *B bifidum*, *L acidophilus*, *L casei*)	IRT5 decreases symptoms of myasthenia gravis by "inhibiting the infiltration of complement component and loss of AChR contents at NMJ. Treatment with IRT5 probiotics further suppressed AChR reactive immune responses and down-regulated the levels of pro-inflammatory cytokines (IFN-γ, TNF-α, IL-6 and IL-17)."[45] Further, this probiotic blend decreased autoantibody levels. IRT5 probiotics (*S thermophiles*, *L reuteri*, *B bifidum*, *L acidophilus*, *L casei*) suppress immune disorders by creation of CD4+FOXP3+ Tregs.	**IRT5 probiotics:** Mega Flora Plus (Mega Food) Flora 50-14 and Flora 20-14 (Innate Response) Strengtia (Apex Energetics)	**IRT5 probiotics:** Similar to mixtures used in many kefirs and yogurts.
Autoimmune Encephalomyelitis				
Lavasani et al[46] (2010)	*L paracasei* DSM 13434, *L plantarum* DSM 15312 and 15313	*L paracasei* DSM-13434, *L plantarum* DSM-15312, and DSM-15313 decreased inflammation in the central nervous system. *L paracasei* and *L plantarum* DSM-15312 caused CD4+CD25+FOXP3+ regulatory T cells to be induced and also increased production of serum TGF-β1. Serum IL-27 was increased with use of *L plantarum* DSM-15313. Use of *L paracasei* DSM-13434, and *L plantarum* DSM-15312 and DSM-15313 appeared to decrease signs and symptoms of autoimmune encephalomyelitis. "Our data revealed that the suppressed activity was associated with reduced inflammation in CNS, down-regulation of MOG-induced T cell responses and a shift in production of pro-inflammatory cytokines toward the beneficial Th2 type response including IL-4, IL-10 and TGF-β1."	***L paracasei* DSM-13434:** Not available. ***L plantarum* DSM 15312 and 15313:** Not available.	None
General Immune/Autoimmune				
Issazadeh-Navikas et al[7] (2012)	*L plantarum*, *L reuteri*, *L casei*	*L plantarum* blocks proteasome function blocking the break-down of NF-kB, which influences Treg cells. *L plantarum*, *L reuteri*, and *L casei* activate dendritic cells allowing for conversion of T cells to Treg cells.	***L plantarum*:** Biotics Research Biodolph 7-Plus Sibiotica (Apex Energetics) ***L rhamnosus* GR-1 and *L reuteri* RC-14:** UltraFlora Women's Fem-Dophilus (Jarrow Formulas) ***L casei*:** PerioBiotic Toothpaste (Designs for Health) ***L casei* and *L plantarum*:** Klaire Labs Ther-Biotic Complete Sibiotica (Apex Energetics)	***L plantarum*:** Fermented vegetables, Kevita probiotic drinks, olives (green) ***L reuteri*:** None ***L casei*:** Kefir, kvass, lassi, yogurt
Chervonsky[3] (2011)	*B fragilis*	*B fragilis* contains a bacterial polysaccharide (polysaccharide A) that stimulates immune response and can suppress reaction of the immune system. Various bacteria strains exert effects on anti-inflammatory cytokines such as IL-10 and suppressive Treg cells. Segmented filamentous bacteria induce T_h17 in mice models, a proinflammatory T-helper cell. Microbiota serve as a means of "colonization resistance," preventing various infections such as *S typhimurium*.	***B fragilis*:** Not available.	***B fragilis*:** None

Table 1. (continued)

Immune Conditions	Strains	Overview	Professional and Commercial Products	Foods
Richards et al[1] (2016)	SCFA	Production of SCFA provides health benefits such as decreasing inflammation and improving homeostasis of the metabolism. SCFAs exert influence on immune cells located near the lymphoid compartments of the gut and can move systemically to influence tissues in the periphery. High-fiber foods positively affect the immune system and microbiota by providing an energy source for microbial communities, which then influence the immune and metabolic homeostasis. The SCFA acetate appears to provide immune benefits and protection from pathogens helping to prevent intestinal permeability associated with autoimmune disease. SCFAs are anti-inflammatory and immunomodulatory, because they promote Treg cells allowing for better immune tolerance. The Treg cells then produce IL-10 after TGF-β cytokine exposure in the periphery from naïve $CD4^+$ T cells. SCFAs influence autoreactive cells, such as B cells related to inflammatory disease, such as lupus and type 1 diabetes via their production of autoantibodies.	Probiotics that contain prebiotics.	High-fiber foods
Kverka et al[30] (2012)		Probiotics can influence the microbiome by influencing production of antimicrobial peptides in the hosts and improving barrier function, and they have immunomodulatory properties at most levels of regulation such as downregulation of PRRs expression, NF-kB signaling, and proinflammatory cytokine production.		
Reynolds et al[47] (2016)	*B fragilis*, *B infantis*, *Clostridium* spp, *Lactobacillus* spp	*B fragilis*, *B infantis*, *Clostridium* spp, and *Lactobacillus* spp induce production of suppressive Tregs.	*Lactobacillus* found in most commercially available probiotic supplements. ***B infantis*:** Mega Flora (Mega Food) Innate Flora 5-14 Complete Care	*Lactobacillus* commonly found in fermented foods and beverages. ***B infantis*:** None

Note: Several other conditions are autoimmune in nature; however, they have been covered extensively in other portions of this comprehensive review. Please see the additional articles of this series for specific conditions, as outlined in the abstract.

Abbreviations: GALT, galactose-1-phosphate uridylyltransferase; IFN-ɣ, interferon gamma; IgA, immunoglobulin A; IgE, immunoglobulin E; IgM, immunoglobulin M; IL, interleukin; NF-kB, nuclear factor kappa B; NOD, nonobese diabetic; OVA, ovalbumin; PRRs, pattern recognition receptors; RA, rheumatoid arthritis; RCT, randomized clinical trial; SCFA, short-chain fatty acid; SLE, systemic lupus erythematosus; SNAS, systemic nickel allergy syndrome; TGF, transforming growth factor; T_h1, T-helper 1; T_h2, T-helper 2; TNF-α, tumor necrosis factor alpha; Treg, T-regulatory.

Research Overview: Immune Conditions

There is a significant difference in beneficial bacteria levels in healthy children with a genetic predisposition to type 1 diabetes as compared with those who have type 1 diabetes. Healthy children have high levels of *Lactobacillus* and *Firmicutes*, whereas unhealthy children have higher levels of *Bacteroides*.[8] Early probiotic supplementation may then play a protective role against the development of type 1 diabetes.

In one study, children with the DR3/4 genotype, a genotype that increases the risk of diabetes development, were provided early supplementation with probiotics from ages 0 to 27 days of life. This appeared to decrease the risk of type 1 diabetes compared with infants given probiotics after 17 days or when no probiotics were given at all. Supplements given to study participants included mixtures of various *Lactobacillus* and *Bifidobacterium* species. The authors speculated that the ineffectiveness of probiotics when given beyond 27 days of life is likely from the influence of diet on the microbiome.[9]

As part of the PRODIA Study, Ljungberg et al[10] sought to determine whether probiotics given during the first 6 months of life could decrease the onset of type 1 diabetes in children at risk genetically for the disease. The initial pilot study assessed 200 subjects at 6, 12, and 24 months of age to look at the presence of autoantibodies. In addition, the authors were considering the feasibility of the protocol and whether it might be used in a subsequent study. Although there was a high dropout rate (between 15% and 25%) due to parents not wanting to participate, the authors believed that the PRODIA protocol was feasible. Probiotics used in this trial included *L rhamnosus* GG (5×109 CFU), *L rhamnosus* LC705 (5×109 CFU), *Bifidobacterium breve* BBI99 (2×108 CFU), and *Propionibacterium freudenreichii* subsp Shermanni (2×109 CFU). During the study, one subject developed diabetes at 6 months of age and 2 subjects at 24 months of age.

Systemic lupus erythematosus (SLE) appears to be influenced by a decreased ratio of *Firmicutes* to

Bacteroidetes. In SLE, IFN-ɣ (T_h1 cytokine) levels were negatively associated with *Bacteroidetes* and positively associated with *Firmicutes* and the *Firmicutes*:*Bacteroidetes* ratio. The induction of Treg cells by species including *Bifidobacterium bifidum* LMG13195, *Ruminococcus obeum* DSM25238, and *Blautia coccoides* DSM935 help to balance the immune system, providing protection against SLE development. On the other hand, *Synergistes* were correlated in SLE with serum levels of proinflammatory and T_h17-promoting cytokine IL-6, which is associated with a humoral immune response. They may also promote immunoglobulin M antibodies, which could be decreased in SLE.[11]

Unlike healthy controls, patients with rheumatoid arthritis (RA) have significantly less bifidobacteria, bacteria from the *Bacteroides-Porphyromonas-Prevotella* group, *Bacteroides fragilis* subgroup, and *Eubacterium rectale-Clostridium coccoides* group. Bacteria generally found in the oral cavity, including *Porphyromonas gingivalis* and *Prevotella intermedia*, can be found in the synovial fluid of patients with RA. Antigen-specific antibodies are also found against *P gingivalis*, *P intermedia*, and *Bacteroides forsythus* in these patients.[12] Species including *L casei*, *Bacillus coagulans* GBI-30 and 686, *L rhamnosus* GR-1, *L reuteri* R-14, *Lactobacillus* GG, *Lactobacillus fermentum*, *Lactobacillus delbrueckii*, and *Lactobacillus acidophilus* provide protection against RA by immunomodulation allowing a shift away from the T_h1 immune response that causes RA. For example, in a 12-week study, *L casei* decreased signs of arthritis infiltration of lymphocytes into the joint and cartilage breakdown in a rat model. Further, decreased levels of proinflammatory cytokines and decreased T-cell proliferation were found in combination with increased levels of the anti-inflammatory IL-10.[13]

Whereas beneficial microbiota decrease risk for autoimmunity by shifting cellular immunity toward T_h1, the opposite occurs to help prevent allergic response. For example, *L casei* Shirota helps to improve cellular immunity by modulating the T_h1/ T_h2 balance toward T_h1 improving the allergic response.[14] Other similar species, found in autoimmunity, simply influence the generation of Treg cells. This includes *L rhamnosus* GG, *B lactis, L casei* DN-114001, *L salivarius*, and *L reuteri* ATCC23272.[7] Alternately, probiotics may positively benefit the allergic response by inhibition of immunoglobulin E (IgE) production.[15] Similarly, *Lactobacillus* GG and *L rhamnosus* LC705 suppress genes encoding FCER1A and FCER1G, which encode allergy-related high-affinity IgE receptor units α and γ, respectively, and also suppress the histamine H_4 receptor. They work by decreasing proinflammatory mediators such as IL-8 and tumor necrosis factor alpha (TNF-α), while upregulating the anti-inflammatory IL-10.[16] Other strains, such as *L casei* DN-114-001, help stabilize mast cell degranulation and subsequent release of mediators including histamine and heparin, which prevent secretion of IL-5, IL-6, IL-13, TNF-α, MCP-1, and MIP-1α. These are the 4 cytokines and 2 chemokines that induce FCER1 aggregation.[17]

L reuteri DSM17938 has been found to be useful for those experiencing atopic dermatitis, gastrointestinal symptoms, and intestinal permeability. In a study by Randazzo et al,[18] the authors investigated this strain to explore whether it would provide protection for those with systemic nickel allergy syndrome (SNAS) in which contact with nickel causes chronic and recurrent issues with inflammatory skin disease. Nickel is found in most food items and causes urticaria, angioedema, flares, itching, meteorism, colic, and diarrhea in patients with SNAS. Typically, patients with SNAS are advised to consume a low-nickel diet, which means severely limiting vegetable intake, which can contribute to additional health problems.[18] In a preliminary double-blind randomized placebo-controlled study Randazzo et al,[18] the authors determined that *L reuteri* DSM17938 could decrease symptoms of SNAS. Further, it may help restore diversity within the microbiome, which could also help to further calm the immune system.

Although studies examining probiotics given to young children to prevent IgE allergies have failed to show validity in the general population, they may confer protection to children delivered by cesarean section.[19] A double-blind, placebo-controlled study consisting of 1223 mothers pregnant with infants thought to have substantial risk for allergy were given, during their final month of pregnancy, a probiotic mixture containing a probiotic mixture containing 2 lactobacilli, bifidobacteria, and propionibacteria, or a placebo. The children born to these mothers were also given probiotics from birth through 6 months of age, as well as the prebiotic galactooligosaccharide or placebo. The children were then evaluated at the age of 5 years for allergic conditions such as eczema, food allergy, allergic rhinitis, and asthma. Although again this study showed that there was no difference in general between the active and placebo groups, it was found that there was a decreased rate of IgE-associated allergies in children who were delivered by cesarean section (24.3% vs 40.5%; OR, 0.47; 95% CI, 0.23% to 0.96%; $P = .035$).[19] There did seem to be a significant decrease in IgE-associated allergies in all infants in the study at 2 years of age. The authors believed that this protection was provided by mediators such as IL-6 produced by toll-like receptors that could then induce IgA differentiation for naïve B cells, a common occurrence in infants with eczema after being given probiotics.[19] Infants in this 2009 study were found at 6 months of age to have elevated levels of serum C-reactive protein, IL-10, and IgE at 6 months of age.

Although there is a wealth of information regarding the effect of various microbial species on the immune system and the implications for autoimmunity and allergy, one

should be aware that the vast majority of these studies have been conducted on rat and mouse populations and not on humans. Human randomized controlled trials are greatly needed to help expand clinical knowledge of probiotics so that practitioners may better use probiotics effectively with patients. Further, although research has been conducted for autoimmune diseases such as SLE, RA, type 1 diabetes, and myasthenia gravis, there is a lack of information regarding other autoimmune diseases such as Hashimoto's thyroiditis, Graves' disease, pernicious anemia, alopecia areata, vitiligo, and others. The question of how much one should extrapolate information regarding probiotic's effect on one autoimmune disease to another is another issue that requires addressing in the expanding knowledge base of the microbiome's effect on the immune system.

Nutritional Supplements Overview

Professional and commercial dietary supplements containing probiotics are widely available.[20] In 2002, it was estimated that more than 100 companies in the United States marketed probiotic supplements and nearly 2 million adults consumed them regularly.[21] 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.[22] Using probiotics for general health versus targeting a specific health concern is more complex, because the properties of probiotic species are strain specific.[23] 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.[24] 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. In this multiseries review, it was identified that 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.

Table 2 is designed to be a resource to see what is available "at-a-glance." The brands were chosen by

Table 2. Summary of Nutritional Supplements by Health Concern

Health Concern	Professional and Commercial Products	Strains
Allergy	Advanced Acidophilus Plus (Solgar)	*B lactis* (BB-12)
Allergy	Advanced Acidophilus Plus (Solgar)	*B lactis* (BB-12)
Allergy	Advanced Multi-Billion Dophilus (Solgar)	*Lactobacillus* GG
Allergy	Bifido GI Balance (Life Extension)	*B longum* BB-536
Allergy	Bifilon (Quality of Life Herbs)	*B longum* BB-536
Allergy	BioDoph-7 Plus (Biotics Research)	*S thermophilus*, *L paracasei*
Allergy	Dr. Formulated Probiotics and Primal Defense (Garden of Life)	*L salivarius*
Allergy	Flora products (Innate Response)	*L salivarius*
Allergy	Gr8-Dophilus (NOW Foods)	*L salivarius*
Allergy	ImmuProbio (Health Aid)	*L acidophilus*, *L bulgaricus*, *B bifidum*, *B longum*
Allergy	Innate Flora 5-14 (Complete Care)	*B longum*
Allergy	Jarr-Dophilus EPS 25 Billion (Jarrow Formulas)	*L lactis*
Allergy	Jarro-Dophilus EPS and Baby's Jarro-Dophilus+FOS Powder (Jarrow Formulas)	*B longum* BB536
Allergy	Lactobacillus Gasseri 3 Billon CFU (Swanson)	*L gasseri*
Allergy	Mega Flora (Mega Foods)	*B longum*
Allergy	Mutaflor (Tribute Pharmaceuticals); contains the Nissle 1917 strain	*E coli*
Allergy	Not available	*L casei* Shirota, DN-114 001 and YIT9029
Allergy	Not available	*L rhamnosus* GG (ATCC53103), JB-1
Allergy	Not available	*L reuteri* (ATCC23272)
Allergy	Not available	*L casei* DN-114001
Allergy	Not available	*L reuteri* DSM 122460
Allergy	Not available	*L rhamnosus* 19070-2, LC705
Allergy	Not available	*L brevis* HY7401
Allergy	Not available	*L plantarum* HY20301
Allergy	Not available	*L salivarius* LS01
Allergy	Not available	*B fragilis*
Allergy	One-A-Day TruBiotics (Bayer)	*B lactis* (BB-12)
Allergy	One-A-Day TruBiotics (Bayer)	*B lactis* (BB-12)
Allergy	Perfect Biotics (Probiotic America)	*L lactis*
Allergy	ProSynbiotic (Standard Process)	*B lactis* (BB-12)
Allergy	ProSynbiotic (Standard Process)	*B lactis* (BB-12)
Allergy	RAW Probiotics Women 85 Billion CFU (Garden of Life)	*L lactis*
Allergy	SymBiotics with FOS Description (Nutricology)	*S thermophilus*
Allergy	Tribif (Valeas)	*B longum* BB536
Allergy	Ultra Strength Probiotic 10 (Nature's Bounty)	*L salivarius*
Allergy	UltraFlora Spectrum (Metagenics)	*L salivarius*
Allergy	Walgreens Probiotic *Lactobacillus* GG	*Lactobacillus* GG
Autoimmune Encephalomyelitis	Not available	*L paracasei* DSM-13434
Autoimmune Encephalomyelitis	Not available	*L plantarum* DSM-15312 and DSM15313
General Immune/ Autoimmune	Biotics Research Biodolph 7-Plus	*L plantarum*
General Immune/ Autoimmune	Fem-Dophilus (Jarrow Formulas)	*L rhamnosus* GR-1, *L reuteri* RC-14
General Immune/ Autoimmune	Klaire Labs Ther-Biotic Complete	*L casei*, *L plantarum*
General Immune/ Autoimmune	Not available	*B fragilis*
General Immune/ Autoimmune	PerioBiotic (Toothpaste-Designs for Health)	*L casei*
General Immune/ Autoimmune	UltraFlora Women's	*L rhamnosus* GR-1, *L reuteri* RC-14
Multiple Sclerosis	Flora 50-14 and Flora 20-14 (Innate Response)	*L casei*, *L acidophilus*, *L reuteri*, *B bifidum*, *S thermophiles* combined

Table 2. (continued)

Health Concern	Professional and Commercial Products	Strains
Multiple Sclerosis	IRT5 probiotic powder	*L casei*, *L acidophilus*, *L reuteri*, *B bifidum*, *S thermophiles* combined
Multiple Sclerosis	Isolated for research purpose; not commercially available.	*T suis* ova
Multiple Sclerosis	Mega Flora Plus (Mega Food)	*L casei*, *L acidophilus*, *L reuteri*, *B bifidum*, *S thermophiles* combined
Myasthenia Gravis	Flora 50-14 and Flora 20-14 (Innate Response)	IRT5 probiotics
Myasthenia Gravis	Mega Flora Plus (Mega Food)	IRT5 probiotics
Rheumatoid Arthritis	Advanced Multi-Billion Dophilus (Solgar)	*Lactobacillus* GG
Rheumatoid Arthritis	Flora 50-14 and Flora 20-14 (Innate Response)	IRT5 probiotics
Rheumatoid Arthritis	Klaire Labs Ther-Biotic Complete	IRT5 probiotics
Rheumatoid Arthritis	Mega Flora Plus (Mega Food)	IRT5 probiotics
Rheumatoid Arthritis	Walgreens Probiotic *Lactobacillus* GG	*Lactobacillus* GG
Systemic Lupus Erythematosus	Isolated and cultured for research purposes.	*B bifidum* LMG13195 (Bb)
Systemic Lupus Erythematosus	Not available	*R obeum* DSM25238, *B coccoides* DSM935
Type 1 Diabetes	Dophilus EPS (Jarrow Formulas)	*L casei*
Type 1 Diabetes	Gr8-Dophilus (Now Foods)	*L casei*
Type 1 Diabetes	Isolated from BB-DR rats for research purposes and not available commercially.	*L johnsonii* N62
Type 1 Diabetes	Primal Defense HSO (Garden of Life)	*L casei*
Type 1 Diabetes	Ther-Biotic Factor 4 (Bifidobacterium Complex) 60c by Klaire Labs	*B breve*
Type 1 Diabetes	Udo's Choice Super 5 Probiotic Flora	*L casei*
Type 1 Diabetes	Ultra Jarro-Dophilus (Jarro-Dophilus + FOS, Jarro Formulas)	*L casei*
Type 1 Diabetes	VSL#3 (Sigma-tau Pharmaceuticals, Inc): *B longum*, *B infantis*, *B breve*, *L acidophilus*, *L casei*, *L delbrueckii* subsp, *L bulgaricus*, *L plantarum*, and *S salivarius* subsp Thermophiles	*B breve*

searching the probiotic strain and strain species using Google, several supplement companies, Probiotics Advisor,[25] and the Clinical Guide to Probiotic Products.[26] 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 whether the formula contains a specific species.

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