THE MEDICAL THOUGHT

Probiotics: Immunomodulation and clinical research.

"Student contribution"

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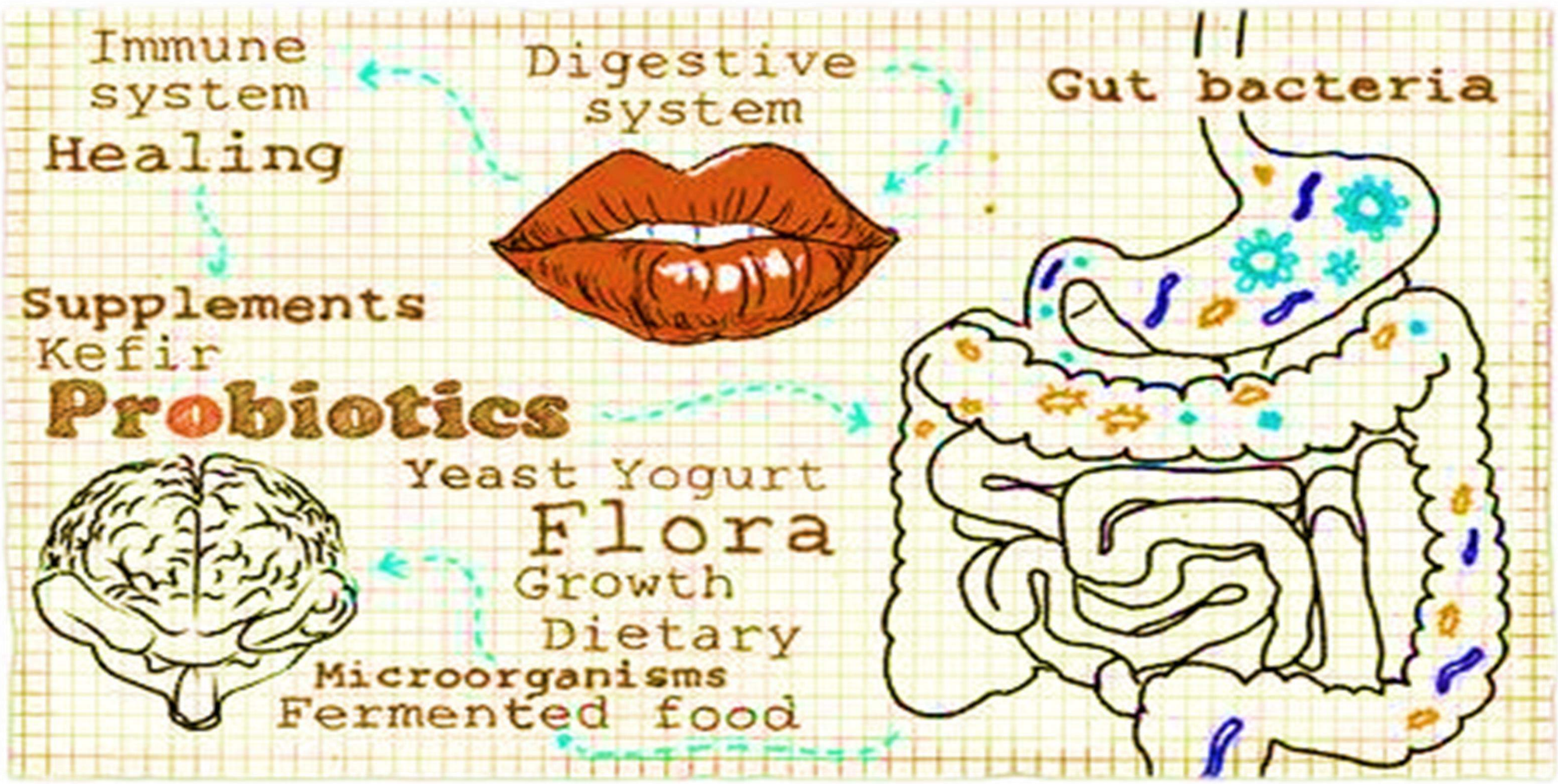
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Systemic lupus erythematosus.



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Probiotics and Prebiotics.

Microbiota (or the microbiome) refers to a collection of microbes that naturally inhabit any particular space. It is a huge and complex ecosystem. Over 100 trillion microorganisms make up our microbiome which means that our personal genes are outnumbered 100:1 by the microbiome gene pool (1,2).

Probiotics are microbes that confer health benefits. Bifidobacterium and Lactobacillus are the most widely recognized probiotic bacteria. The history of the oral consumption of micro-organisms producing a protective effect on the gut flora began a very long time ago with fermented foods (2,3).

Over the last two decades there has been growing interest on both basic and clinical science in probiotics which has resulted in over 6000 publications in the biomedical literature, with over 60% published in the last 5 years, some in the top ranking scientific journals (3,4).

The type of the microbes used as Probiotics increased due to the increase in the research concerning the subject as well as by the increase of the newly discovered and identified microbes, which could be used as Probiotics (3,5).

According to the Food and Agriculture Organisation of the United Nations (FAO) and the World Health Organisation (WHO) probiotics are defined as live microorganisms, which when administered in adequate amounts, confer a health benefit on the host (1,5).

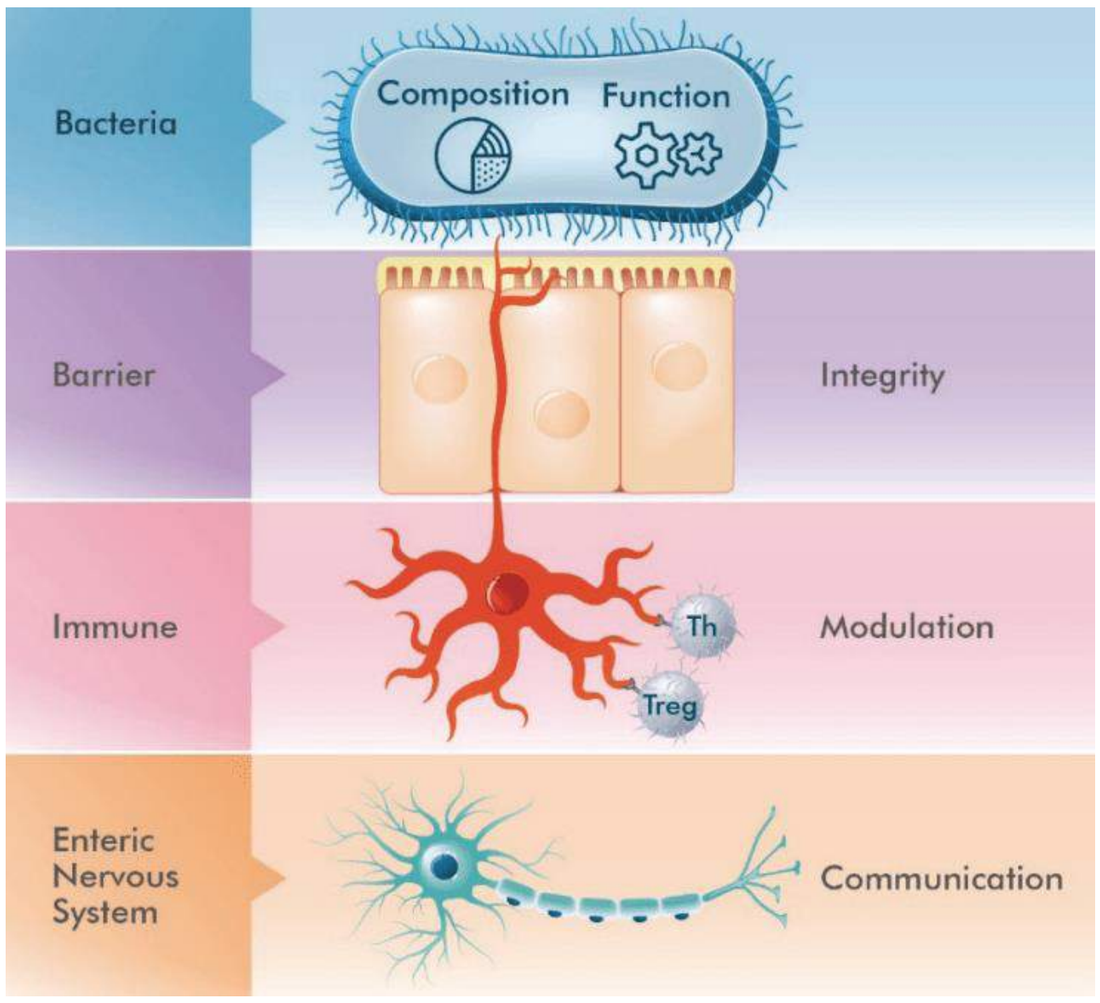
The best probiotic supplements and foods will improve the beneficial bacteria to help crowd out the opportunistic bacteria, boost the immune system to protect against pathogenic bacteria, as well as break down fibrous foods into more digestible components and help your body produce vitamins such as K and B12 (5,6).

The probiotic industry exceeds $4 billion per year currently.

Our bodies have groups of microbes each working collectively to perform different functions. The most important ones are those existing in our digestive system. They improve food digestion and consumption. They are able to complement many deficiencies in our digestive system (6).

Probiotics provide the potential to compensate for the pathological problems of gut dysbiosis and restore balance to the microbiota of the intestinal tract (7).

Credits: Planet Naturopath
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Probiotics are being investigated for the treatment of autoimmune disease by re-balancing dysbiosis induced changes in the immune system. Pregnancy is a health concern surrounding autoimmune disease, both for the mother and her child. Probiotics for maternity are emerging on the market and have gained significant momentum in the literature. Thus far, evidence supports that probiotics alter the structure of the normal microbiota and the microbiota changes significantly during pregnancy (8).

The interaction between probiotics-induced changes and normal changes during pregnancy is poorly understood. Furthermore, there is emerging evidence that the maternal gut microbiota influences the microbiota of offspring, leading to questions on how maternal probiotics may influence the health of neonates. Underpinning the development and balance of the immune system, the microbiota, especially that of the gut, is significantly important, and dysbiosis is an agent of immune dysregulation and autoimmunity (8).

Most probiotic strains of bacteria are gram positive bacteria, meaning that they will interact with Toll-like receptor (TLR)-2, responsible for recognition of bacterial peptidoglycan, and produce pro-inflammatory cytokines, such as IL-6 (8).

Several studies have shown that TLR2 is upregulated in macrophages and epithelial cells after treatment with probiotic species (9).

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Therefore, down regulation of pro-inflammatory cytokine production resultant from activation of NF-kB may be dependent on TLR2 stimulation. Actually, probiotic treatment upregulates anti-inflammatory molecules such as IL-10 and TGF-β and downregulates pro-inflammatory molecules such as IL-8, IL-1β, and TNF-α (10).

Probiotics also modulate the adaptive immune system by increasing the ratio of regulatory to effector T cell populations (11).

Furthermore, some probiotics beneficially enhance B cell responses. Asthma patients treated with Clostridium butyricum enhanced immunotherapy by improving serum-specific IgE, increasing IL-10 producing B cells, and enhancing antigen specificity in peripheral blood B cells (11,12).

L. plantarumstrain AYA was similarly found to increase differentiation of IgA producing B cells into plasma cells resulting in increased IgA production in the small intestine and lung, thus providing protection against infections (13).

Dysregulation of commensal microbial communities and interactions with pathogens are an emerging hallmark of autoimmune disease. Autoimmune disorders are believed to result from genetic predisposition and interactions with the environment (14).

One role of probiotics in dampening autoimmunity is through enhancing gut barrier function. Leaky gut, a condition characterized by a disrupted epithelial layer, is caused by loosening of the tight junction proteins that hold a contiguous barrier in the gastrointestinal tract, and results in penetration of foreign antigens and harmful substances (15). The capacity for probiotics, prebiotics, and metabolites to enhance gut epithelial barrier function is an indication for their effectiveness in treating autoimmune diseases.

Probiotics have been shown to be beneficial in a number of autoimmune diseases. In Systemic Lupus Erythematosus (SLE), the ratio of Th17 to Treg cells is increased, but can be restored by probiotic mixture of Lactobacillus species (16,17).

There is growing evidence supporting the immunomodulatory ability of some probiotics. Several experimental and clinical studies have been shown beneficial effect of some probiotic bacteria, particularly Lactobacillus and Bifidobacteria strains, on inflammatory and autoimmune diseases (18).

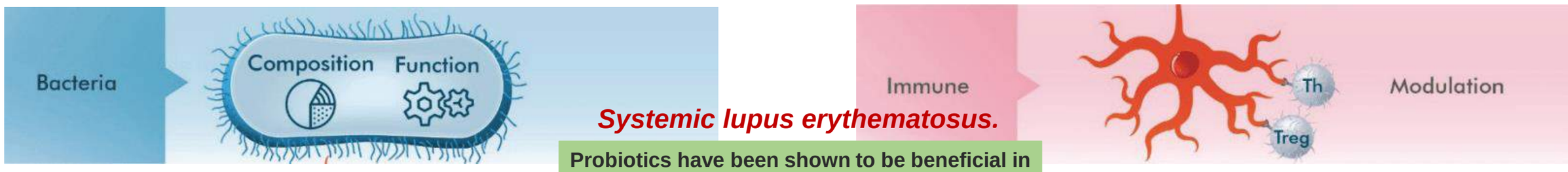
Systemic lupus erythematosus (SLE) is an autoimmune disease that is mainly characterized by immune intolerance towards self-antigens. Some immunomodulatory probiotics have been found to regulate immune responses via tolerogenic mechanisms. Dendritic and T regulatory (Treg) cells, IL-6, IFN-γ, IL-17, and IL-23 can be considered as the most determinant dysregulated mediators in tolerogenic status (18).

As demonstrated by documented experimental and clinical trials on inflammatory and autoimmune diseases, a number of probiotic bacterial strains can restore tolerance in host through modification of such dysregulated mediators (18).

In both animal trials and human trials, probiotics have been investigated to determine potential beneficial effects in the prevention and treatment of a wide variety of systemic conditions. These conditions include inflammatory and autoimmune diseases such as rheumatoid arthritis, ulcerative colitis, multiple sclerosis, and hepatic encephalopathy. Advantages of probiotics include the regulation of immune system function, which is often dependent on the strain of probiotic bacteria. Some strains have demonstrated stimulation of the immune response, thereby being beneficial to patients suffering from immunodeficiency (19).

In a classic hypothesis regarding the etiology of lupus in 1964, Kingsley Stevens pointed out that polysaccharide-containing antigens were 60-fold more effective stimulators of plasma cell proliferation and antibody formation than were the protein antigens present in vaccines. He went on to propose that “the causative agent in SLE” is a bacterial polysaccharide, which must be present in the oropharynx, vagina, or gut. In humans with SLE, elevated interferon-gamma has been found to be proportional to the fecal firmicutes/ bacteroides level, giving credence to Stevens’ hypothesis (20,21).

In this study, several strains of probiotics were helpful in the modulation of excessive inflammatory responses in vitro. Both experimental and clinical trials have revealed that selective strains of probiotics (B. bifidum, Ruminococcus obeum, Blautia coccoides, and L. casei strain Shirota) can reduce inflammation and restore tolerance in SLE animal models (21,22).



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Conflicts of Interest: The authors declare no conflict of interest.

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