To enhance antibacterial and anti-inflammatory activities of the intestinal epithelium, probiotics stimulate cytoprotective protective protein synthesis and secretion, including heat shock protein, defensin, angiogenin, and mucin by intestinal epithelial cells. Recent studies provide significant evidence that probiotics and probiotic-derived soluble factor prevent cytokine and chemical-induced epithelial apoptosis and disruption of barrier function. *Bifidobacterium infantis*-conditioned medium enhances intestinal epithelial barrier function in experimental colitis and prevents cytokine-induced disruption of tight junctions through regulating MAPK activation and tight junction protein expression.

NF-κB signalling is a critical mediator of intestinal epithelial cell crosstalk with immune cells. Optimal NF-κB activity plays a significant role in maintaining normal intestinal homeostasis and injury repair responses. However, hyperactivation of NF-κB results in chronic intestinal inflammatory disorders. One mechanism of probiotic effects is through the suppression of NF-κB signalling to limit excessive inflammation. Soluble factors released by *Bifidobacterium breve* C50 in the culture supernatant reduce TNF-induced cytokine production through inhibition of NF-κB and activator protein 1-dependent transcription in intestinal epithelial cells. These soluble factors and soluble factors-conditioned dendritic cells prevent trinitrobenzene sulfonic acid-induced colitis in mice. However, these effects were not found in response to *B. breve* ATCC 15698, *L. rhamnosus* ATCC 10863, and *Eubacterium rectale* L15. Yet, factors present in conditioned media of *Lactobacillus plantarum*, but not *L. acidophilus, L. paracasei, B. fragilis, B. breve, E. coli* F18 or enteropathogenic *E. coli,* inhibit TNF-induced NF-κB-binding capacity, IκB degradation, and proteasome activity in intestinal epithelial cells, macrophages, and dendritic cells. These studies indicate probiotic strain-specific secretion of factors regulate NF-κB activation.

Probiotic immunoregulatory effects independent of NF-κB have also been reported. *E. coli* Nissle 1917 expresses a direct anti-inflammatory activity on human epithelial cells via a secreted factor, which suppresses TNF-induced interleukin (IL)-8 transactivation, which occurs in the absence of NF-κB inhibition.

Quick Facts

Probiotics are not the same thing as **prebiotics** - non-digestible food ingredients that selectively stimulate the growth and/or activity of beneficial microorganisms already in people's colons. When probiotics and prebiotics are mixed together, they form a **synbiotic.**

Intestinal Immune Responses

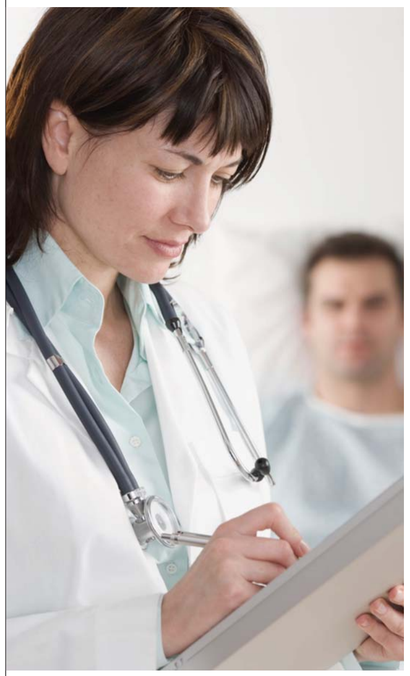
Both in-vitro and in-vivo studies have shown effects of probiotics on defining and maintaining the delicate balance between necessary and excessive defense mechanisms, including innate and adaptive immune responses; upregulation of immune function may improve the ability to fight infections; downregulation may prevent the onset of intestinal inflammation and autoimmunity. Previous studies have demonstrated that probiotics perform these immunoregulatory effects through enhancing innate immunity, promoting anti-inflammatory, and inhibiting pro-inflammatory cytokine production. Activation of Toll-like receptor-regulated signalling is one of the known mechanisms for probiotic regulation of immune functions.

Studies focusing on immunoregulatory effects of probiotics on colitis show that the mixture of *L. acidophilus* and *Bifidobacterium longum* prevents experimental colitis through expansion of intestinal intraepithelial γσT cells and regulatory T cells (Treg), as well as downregulation of pro-inflammatory cytokines, TNF, and monocyte chemotactic protein 1 and upregulation of the anti-inflammatory cytokine IL-10. In another in-vivo study, *B. infantis* drives the generation and function of Treg cells to suppress lipopolysaccharide (LPS)-induced NF-κB activation and *Salmonella typhimurium* infection.

Furthermore, several probiotic-derived factors mediate probiotic function in immunity. For example, *Lactobacillus reuteri* secreted factors promote TNF-induced apoptosis and antiapoptotic protein production (Bcl-2 and Bcl-xL) in human myeloid cells by inhibiting NF-κB activation and enhancing MAPK signalling. Two identified factors of probiotics have been reported. S layer protein A of *L. acidophilus* NCFM promotes dendritic cell maturation and function to stimulate T helper cell 2 T-cell polarization. Polysaccharide A, made by *B. fragilis,* protects against experimental colitis through inducing IL-10 production.

Conclusion

Understanding probiotic action may permit modulation of the immune system, both locally and systemically. Knowledge of probiotics on the host immune system has entered a new and fascinating phase of research and progression in this field is likely to offer novel and useful means to modulate host immunity for protection from, or treatment of, a wide variety of human disorders, like inflammatory bowel disease.



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Printed by Chin Hiap Hong Corporation Pte Ltd

August 2011 Issue 7

The Probiotics news

MICA (P) 168/06/2011

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An educational project by MD Pharmaceuticals Pte Ltd

Message from the Editor

In this 7th issue, we would like to thank Dr Mary Ellen Sanders for her educational article on probiotic microbiology. Dr Sanders is the Executive Director of the International Scientific Association for Probiotics and Prebiotics (ISAPP) and had also served on the World Gastroenterology Organization Guidelines Committee preparing guidelines for the use of probiotics and prebiotics for gastroenterologists.

Our readers will also benefit from an article on childhood constipation as this complaint is quite frequently brought up by many young couples to their respective family doctors.

Understanding the mechanisms of action of probiotic should be informative to many physicians as they look towards evidence based probiotic products.

God Bless!

Melvin Wong
Editor-in-chief

Perspectives on a Quality Probiotic

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Introduction

Probiotics are live microorganisms, which when administered in adequate amount confer a health benefit on the host. The range of probiotic products is increasing globally. However, not all products labelled "probiotic" meet the criteria for a quality product. Although it is difficult for consumers to differentiate among the commercial products available, some key attributes to look for in probiotics may guide this effort (Sanders, 2009).

Key Attributes of Probiotics

A probiotic is a microbe. Bacteria and yeast have been studied as probiotics. Bacteria used for probiotics include strains of *Lactobacillus* species, *Bifidobacterium* species, *Streptococcus thermophilus, Bacillus* species and *Escherichia coli.* A variant of *Saccharomyces cerevisiae,* S. boulardii, has also been used as a probiotic. Live viruses used for vaccines are considered outside the realm of probiotics.

A probiotic must be alive when administered. However, a probiotic may die after administration to the host. Viability at the site of action is presumed to be important, but some effects may be mediated by cell components. Recovery of the fed strain in faeces is suggestive that the microbe is alive at active sites within the alimentary canal.