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Screening and Development of Probiotic Bacteria with Improved Health Functions

Geun Eog Ji

Department of Food and Nutrition, Seoul National University

Bifidobacterium spp. is nonpathogenic, Gram-positive and anaerobic bacteria which inhabit the intestinal tracts of humans and animals. In breast-fed infants, bifidobacteria comprise more than 90% of the gut bacterial population. *Bifidobacterium* strains are used in commercial fermented dairy products and various probiotic products and have been suggested to exert health promoting effects on the host by maintaining intestinal microflora balances, improving lactose tolerance, increasing synthesis of vitamins, and aiding the immune enhancement and anticarcinogenic activity for the host. The beneficial effects of the probiotic strains are known to be strain-specific. The adhesion of probiotic bacteria to the intestinal mucosa is one of the desirable properties for their colonization in the intestinal tract where these bacteria constantly compete with other bacteria. The adhesion of different strains of bifidobacteria to Caco-2 cells was compared. Among them, strain BGN-4 showed the highest adhesion. In our laboratory a selected strain *B. bifidum* BGN4 showed a strong adhesion to a human enterocyte cell line, Caco-2, and anti-tumor effect in the *in vitro* and *in vivo* animal models. The adhesive ability and anti-tumor activity of the *B. bifidum* BGN4 were improved when grown in the presence of phytic acid. We assessed the efficacies of the probiotic products against the occurrences of the atopy in young infants and of the irritable bowel sydrome in adults, respectively, in double-blind, randomized placebo-controlled human trials. Probiotics-treated infants group administered with combination of *B. bifidum* BGN4, *B. lactis* AD011 and *Lactobacillus acidophilus* AD031 showed the prevalence of AD at 6-12 months, 18.2% in probiotics group versus 40.0% in placebo group (p=0.048), and the cumulative incidence of AD at 12 months was reduced significantly in probiotics group (36.4% vs. 62.9, p=0.029). The administration of probiotcs (*B. bifidum* BGN4, *B. lactis* AD011, *L. acidophilus* AD031, and *L. casei* IBS041) lowered the pain score significantly in irritable bowel syndrome patients and increased the bowel movement comfortability when assessed at 4 weeks and 8 weeks after administration. Further supports of the immunomodulatory effect of the probiotics were shown in animal models and *in vitro* cell culture assays. A novel anti-tumor bioactive compound was

purified from *B. bifidum* BGN4 and identified as a polysaccharide BB-pol. DNA microarray showed that BB-pol treatment down-regulated the genes belonging to protein-tyrosine kinases, protein-tyrosine phosphatases, signal transduction-related genes, transcriptional regulators, and transporters, etc. and up-regulated tumor suppressor genes such as TGFBR2 and BIN1.

Rotavirus is the major causative infectious agent of the diarrhea in children during winter and is estimated to cause more than 800,000 annual deaths of young children in developing countries. Several lactic bacteria strains are reported to reduce the duration and severity of symptoms from rotavirus-associated diarrhea. However, the mechanism of action is still not elucidated. In our experiment we isolated a strain which showed a superior anti-rotavirus effect to other various *Bifidobacterium* strains and named the strain as *B. longum* BORI. Anti-rotavirus antibody positive children were randomly assigned into two groups: the probiotics group receiving *Bifidobacterium longum* BORI and *Lactobacillus acidophilus* twice a day and the placebo group. The average age of the participants were 17.8 month in both groups. The stool frequencies were significantly decreased by 3-day administration of probiotics.

Not only lactic bacteria act as probiotics, but also they can produce various biofunctional materials. S-adenosyl-L-methionine (SAM) is an important metabolic intermediate in living organisms and participates in many reactions as a methyl group donor. SAM has been used as a dietary supplement and is proposed to have beneficial effects on the liver and brain. *B. bifidum* BGN4 produced a significantly higher amount of SAM than other *Bifidobacterium* or *Lactobacillus* strains. SAM producing lactic bacteria might be utilized as a source of SAM in the functional food industry. Additionally, bifidocin BK421, a bacteriocin from *Bifidobacterium* was characterized.