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Editorial

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Probiotics, the New Approach for Cancer Prevention and/or Potentialization of Anti-Cancer Treatment?

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Uncontrolled proliferation of the cells and their resistance to programmed cell death are main features of malignant cells. The effectiveness in the treatment of cancers is based on the restoration of the sensitivity of transformed cells to apoptotic signals. Although significant progress has been made in this field during last decades, the resistance to chemotherapy becomes a problem in many cases. The association between cancer and modifiable health behaviors is well supported. At least one-half of all cancers are suggested to have a dietary component. Therefore many of the dietary agents and natural health products have attracted the attention of scientists. One of them is probiotics, the nonpathogenic microorganisms living in the intestinal tract which benefit the host. In human clinical trials, probiotics has been used successfully in the treatment of acute diarrhea. Other clinical indications for probiotics, mainly in inflammatory bowel disease, are still evaluated with promising preliminary data. In addition to regulation of intestinal epithelial homeostasis and immune responses, certain probiotics have been reported to activate anticancer mechanisms. Altonsy et al. described induction of mitochondrial pathway of apoptosis in human colonic carcinoma cells (Caco-2) incubated with probiotics such as *Lactobacillus rhamnosus* or *Bifidobacterium lactis* or commensal bacteria–*Escherichia coli* and *Atopobium minutum* [1]. The results of Baldwin et al. suggested that *Lactobacillus acidophilus* and *Lactobacillus casei* were able to increase the apoptosis-induction capacity of 5-fluorouracil in colorectal carcinoma cell line LS513, suggesting that these probiotics may be used as adjuvants in anticancer chemotherapy [2]. However both studies did not determine whether examined probiotics had similar abilities to affect apoptosis in human normal colon cells. *Propionibacterium freudenreichii* was shown to induce cell death of different human colon and gastric cancer cell lines through secretion of short-chain fatty acids to culture media [3]. Moreover it enhanced the camptothecin cytotoxicity activity, drug used in gastric cancer chemotherapy. As a probiotic fermented milk may be used to prevent gastric cancer and/or to potentialize therapeutic treatments [4]. Another study reported that exopolysaccharides (EPS) of *Lactobacillus acidophilus* were involved in colon cancer cell death via autophagy [5]. It has been suggested that synbiotic (mixture of probiotic and prebiotics-substrate for fermentation by the microbiota), might be more active than either a probiotic or prebiotic alone in preventing colorectal cancers [6]. Le Leu et al. demonstrated that combination of prebiotic (resistant starch, RS) and *Bifidobacterium lactis* significantly facilitated the apoptotic response to a genotoxic carcinogen in the distal colon of rats in a short time after carcinogen exposure. This effect was not observed using RS combined with *L. acidophilus* [7]. Removal of the cells with genomic instability through apoptosis is an important regulatory process in the protection against oncogenesis. Moreover the same group of scientists reported recently that combination of RS and *B. lactis* significantly protected against the development of colorectal cancer in the rat-azoxymethane model [8]. Some of probiotic strains have been reported to influence also hematological cancers. *Lactobacillus reuteri* enhanced TNF-induced apoptosis in human chronic myeloid leukemia-derived cells by modulation of NF-κB and MAPK signaling and reduced proteins that mediated cell proliferation (cyclin D1 and COX-2) or inhibited apoptosis (Bcl-2, Bcl-xL) [9]. Chiu described bacterial soluble factors *(LcrS)* secreted by *Lactobacillus casei rhamnosus* which induced apoptosis of human monocytic leukemia-cell line (THP-1) [10]. Meta-analysis of the efficacy of probiotic supplementation in the prevention and treatment of radiation-induced diarrhea showed its beneficial effect in experimental animal studies. However the results of human clinical trials were not consistent and should be well-preformed as the randomized placebo-controlled studies [11]. It also should be mentioned that clinical application of probiotics has some limitations. Bacteremia associated with probiotic therapy has been already reported in children and immunocompromised patients [12,13]. The risk for developing bacteremia may be decreased by using bacteria products in therapy which showed the similar activity as whole bacteria.

In conclusion, the anticancer activity through induction of apoptosis of cancer cells seems to be promising approach for use of some probiotic strains as a support therapy or disease prevention. Additional *in vivo* studies are necessary to ascertain if results obtained from *in vitro* experiments can be translated to the clinical practice.

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