
Abstract
Yogurt is generally recognized as a beneficial food for our health, but research into its physiological effects has focused mainly on intestinal dysfunctions such as constipation and diarrhea. We previously found yogurt fermented with Lactobacillus delbrueckii ssp. bulgaricus OLL1073R-1 (hereafter OLL1073R-1) could reduce risks of catching the common cold and flu in human trials. It was assumed that immunostimulatory exopolysaccharide (EPS) produced from OLL1073R-1 play an important role in this context. However, few studies have examined the immunostimulatory effects of traditional Bulgarian yogurts fermented with different strains of lactobacilli and their metabolites. Therefore, we screened 139 L. delbrueckii ssp. bulgaricus strains and identified OLL1073R-1 as the most robust producer of EPS. This strain was also the only strain that induced the production of IFN-γ in vitro. Oral administration of the EPS or yogurt fermented with OLL1073R-1 and Streptococcus thermophilus OLS3059 (OLL1073R-1 yogurt) augmented natural killer (NK) cell activity and induced IFN-γ production in spleen cells in mice, whereas 2 other yogurts fermented with other strains had no effect on NK cell activity. Cellular preparations of the OLL1073R-1 strain also slightly augmented NK cell activity, but were less effective than EPS itself. The EPS-dependent stimulation of NK cell activity was abrogated in IFN-γ knockout mice and in myeloid differentiation factor 88 knockout mice. Furthermore, IFN-γ production from spleen cells stimulated with EPS was completely blocked with both anti-IL-12 and anti-IL-18 antibodies in vitro. These findings suggest that NK cell activation by OLL1073R-1 yogurt is EPS-dependent, occurs via IL-12- and IL-18-mediated IFN-γ production, and requires myeloid differentiation factor 88. We showed that traditional Bulgarian yogurt could exert immunostimulatory effects by selecting starter strains and part of the mechanisms depend on IFN-γ inducible EPS produced from L. delbrueckii ssp. bulgaricus. Further investigations on processes of fermentation to increase of the EPS may lead to the development of new functional foods that keep our immune functions stable.