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The effect of alloferon on the enhancement of NK cell cytotoxicity against cancer via the up-regulation of perforin/granzyme B secretion

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Alloferon is a novel immunomodulatory peptide originally isolated from infected insects. It has anti-viral and anti-tumor effects via the activation of NK cells. However, specific mechanisms leading to NK cell activation and anti-tumor responses yet to be clarified. In this study, we demonstrate that alloferon increases killing activity of NK cells to cancer cells via the up-regulation of the expression of NK-activating receptors, 2B4. In addition, the production of IFN-γ and TNF-α and granule exocytosis from NK cells against cancer cell were increased by alloferon. Lastly, the anti-tumor effect of alloferon was confirmed in vivo to demonstrate effective retardation of tumor growth in the human to mouse xenograft model. All taken together, these results suggest that alloferon has anti-tumor effects through up-regulation of NK-activating receptor 2B4 and the enhancement of granule exocytosis from NK cells.

Immune enhancing activity of *Cordyceps militaris* fermented with probiotics *in vitro* and *in vivo*

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The goal of the present study was to investigate the immune-enhancing activity of *C. militaris* grown on germinated soybeans (GSC) fermented with *Pediococcus pentosaceus* (ON89A) (GSC-ON89A). We previously reported that the polysaccharides from GSC have immunostimulatory activities in RAW 264.7 macrophages and anti-viral activities. In this study, the immunostimulatory activities of GSC-ON89A were investigated further using various experimental models such as *in vitro*, *ex vivo* and *in vivo*. Among GSC fermented with probiotics (*Pediococcus pentosaceus* (SC11), *Lactobacillus pentosus* (SC64), *Weisslela cibaria* (spum8), *Lactococcus lactis* (Bro17), *Pediococcus pentosaceus* (SO-024), *Pediococcus pentosaceus* (ON89A), *Pediococcus pentosaceus* (ON188), *Lactobacillus sakei* (sal.cla22), *Weissella cibaria* (Bro22), *Pediococcus pentosaceus* (GO088)), GSC-ON89A induced the highest elevation of nitric oxide (NO) production in RAW264.7 cells. In addition, GSC-ON89A showed higher phagocytic activity than control or GSC in RAW264.7 cells. In primary cultured mouse peritoneal macrophages, the GSC-ON89A was found to significantly increase phagocytic activity, compared to control and GSC. In the normal mice model, the oral administration of GSC-ON89A improved the NO production of peritoneal macrophages, compared to control and GSC. These results indicate that GSC-ON89A stimulates the immune response of macrophage *in vitro* and *in vivo*.