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Anticancer effects and mechanisms of polysaccharide-K (PSK): implications of cancer immunotherapy.

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Abstract

Polysaccharide-K (polysaccharide-Kureha; PSK), also known as krestin, is a unique protein-bound polysaccharide, which has been used as a chemoimmunotherapy agent in the treatment of cancer in Asia for over 30 years. PSK and Polysaccharopeptide (PSP) are both protein-bound polysaccharides which are derived from the CM-101 and COV-1 strains of the fungus Coriolus versicolor by Japanese and Chinese researchers, respectively. Both polysaccharide preparations have documented anticancer activity in vitro, in vivo and in human clinical trials, though PSK has been researched longer and has therefore undergone more thorough laboratory, animal and clinical testing. Several randomized clinical trials have demonstrated that PSK has great potential as an adjuvant cancer therapy agent, with positive results seen in the adjuvant treatment of gastric, esophageal, colorectal, breast and lung cancers. These studies have suggested the efficacy of PSK as an immunotherapy or biological response modifier (BRM). BRMs potentially have the ability to improve the "host versus tumor response," thereby increasing the ability of the host to defend itself from tumor progression. The mechanisms of biological response modification by PSK have yet to be clearly and completely elucidated. Some studies suggest that PSK may act to increase leukocyte activation and response through up-regulation of key cytokines. Indeed, natural killer (NK) and lymphocyte-activated killer (LAK) cell activation has been demonstrated in vivo and in vitro, and recent genetic studies reveal increased expression of key immune cytokines in response to treatment with PSK. An antimetastatic action of PSK has also been demonstrated and is perhaps attributed to its potential to inhibit metalloproteinases and other enzymes involved in metastatic activity. PSK has also been shown to cause differentiation of leukemic cells in vitro, and this effect has been attributed to induction of differentiation cytokines. PSK has further been shown to have antioxidant capacity which may allow it to play a role as a normal tissue chemo- and radio-protector when used in combination with adjuvant or definitive chemotherapy and/or radiotherapy in the treatment of cancer, while it may also enable it to defend the host from oxidative stress. Interestingly, studies have also shown that PSK may actually inhibit carcinogenesis by inhibiting the action of various carcinogens on vulnerable cell lines. This action of PSK may play a role in preventing second primary tumors when an inducing agent, such as tobacco or asbestos, is suspected and may also prevent second malignancies due to the carcinogenic effects of radiotherapy and cytotoxic chemotherapy. Another very important aspect of chemoimmunotherapy, in general is that it may be used on debilitated patients such as those with AIDS and the elderly who might otherwise be denied potentially helpful adjuvant cytotoxic chemotherapy. Further determination of the mechanisms of these anti-cancer, immunostimulating and biological response modifying effects of PSK as well as of other protein-bound polysaccharides is certainly warranted. Indeed, with modern cellular and molecular biology techniques, a better understanding of the specific molecular effects of PSK on tumor cells as well as leukocytes may be determined. Much of the research that has been done on PSK is outlined in this paper and may serve as a foundation toward determining the mechanisms of action of this and other protein-bound polysaccharides in the treatment of cancer. This information may open new doors in the development of novel strategies for the treatment of malignancies using adjuvant immunotherapy in combination with surgery, chemotherapy and/or radiotherapy.

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