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

Fisher M, Yang LX.

Radiobiology Laboratory, St. Mary's Medical Center, California Pacific Medical Center Research Institute, San Francisco 94118, USA.

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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美國加州太平洋醫學中心研究院，聖瑪莉醫學中心，放射生物學系

雲芝中的 PSK 多醣體被亞洲醫學界用作治療癌症的“化療免疫治療劑” (chemoimmunotherapeutic agent) 已達 30
年之久。其中日本和中國的研究人員提取雲芝中的多醣體 PSK 和 PSP
去進行多項試管，動物及人類的臨床抗癌細胞研究。其中雲芝 PSK
被証實對治療胃、食道、直腸、乳腺及肺癌有正面幫助。此外，雲芝 PSK
被確定為有效的“免疫療法劑” (immunotherapeutic agent) 或“生理轉變適應物” (BRM = Biological Response Modifier)。 BRM
可助病人身體去對抗癌細胞病變。這個機制雖仍在研究及分析中，但研究報告指出雲芝 PSK 能增加巨噬細胞 (leukocyte)及“天然殺手細胞” (NK Cells = natural killer
cells)之數量，直接影響癌細胞擴散時的酵素作用，從而減慢癌細胞之擴散活動。

雲芝 PSK亦被研究指出其抗氧化/
保護正常細胞之功能，減輕正常細胞受化療及放射治療產生的副作用帶來的氧化性傷害。雲芝
PSK亦助抑制因煙草尼古丁或石棉引起的第二輪癌症腫瘤生長及預防猛烈的化療/放射治療副作用之發生而危害生命。

由於雲芝 PSK被用作“免疫治療劑”，研究報告亦建議雲芝
PSK是適用於免疫力極低的病人，如：愛滋病病人及不能承受化療的老年人。