Beta 1,3-Glucan Cancer Research

Glucan Source: Yeast	
Citation	Abstract
Vetvicka, V, Terayama K, Mandeville R, Brousseau P, Kournikakis B, Ostroff G **Orally-administered Yeast β1,3-glucan prophylactically protects against anthrax infection and cancer in mice** Journal of the American Nutraceutical Association. Vol. 5, No. 2, Spring 2002: 16-20.	β1,3-glucans from various bacterial, mushroom, yeast, and cereal sources have been establis immunomodulators. In the present paper we demonstrate that orally-administered yeast β1,3-g had significant effects as a prophylactic treatment to reduce the mortality of anthrax infection i In addition, the same type of treatment also inhibited the growth of metastatic cancer cells *in v* The mechanism of action involves the stimulation of three important cytokines: IL-2, IFN-γ, an These results provide preclinical evidence for the beneficial effects of orally-administered yeas β1,3-glucan.
Tokunaka K, Ohno N, Adachi Y, Tanaka S, Tamura H, Yadomae T. **Immunopharmacological and immunotoxicological activities of a water-soluble (1-->3)-beta-D-glucan, CSBG from Candida spp.** Int J Immunopharmacol. 2000 May;22(5):383-94. PMID: 10708886 [PubMed - indexed for MEDLINE]	We have established a convenient, two-step procedure to solubilize the yeast cell wall (1-->3)-beta-D-glucan using the combination of NaClO oxidation and DMSO extraction. Candida soluble beta-D-glucan (CSBG) was mainly composed of a linear beta-1,3 glucan with a linear beta-1,6-glucan moiety. In this study, we screened for several immunopharmacological activities of CSBG and found the following activities: (1) interleukin-6 synthesis of macrophages in vitro; (2) antagonistic effect for zymosan mediated-tumor necrosis factor synthesis of macrophages; (3) augmentation for lipopolysaccharide mediated tumor necrosis factor and nitrogen oxide syntheses of macrophages; (4) activation of alternative pathway of complement; (5) hematopoietic response on cyclophosphamide induced leukopenia; (6) the antitumor effect on ascites form tumor; (7) Enhanced vascular permeability; (8) priming effect on lipopolysaccharide triggered TNF-alpha synthesis; and (9) adjuvant effect on antibody production. These results strongly suggested that CSBG possessed various immunopharmacological activity.
Sveinbjornsson B, Olsen R, Seternes OM, Seljelid R. **Macrophage cytotoxicity against murine meth A sarcoma involves nitric oxide-mediated apoptosis.** Biochem Biophys Res Commun. 1996 Jun 25;223(3):643-9. PMID: 8687449 [PubMed - indexed for MEDLINE]	We have studied the cytotoxic effect of stimulated macrophages on Meth A tumor cells in vitro. When stimulated with interferon-gamma and soluble beta-1,3-D-glucan, macrophages exerted cytotoxicity towards syngeneic Meth A tumor cells. This cytotoxicity was associated with a high level of nitric oxide production. Both cell death and nitric oxide production were significantly inhibited by the addition of aminoguanidine, a specific inhibitor of inducible nitric oxide synthase (iNOS), to the culture medium. The cytotoxic effect was accompanied by internucleosomal cleavage of DNA as shown by electrophoresis and DNA fragmentation assay.

Beta 1,3-Glucan Cancer Research

Glucan Source: Fungal	
Citation	Abstract
Ohno N, Miura NN, Nakajima M, Yadomae T. **Antitumor 1,3-beta-glucan from cultured fruit body of Sparassis crispa.** Biol Pharm Bull. 2000 Jul;23(7):866-72. PMID: 10919368 [PubMed - indexed for MEDLINE]	Sparassis crispa is an edible mushroom recently cultivable in Japan. Polysaccharide fractions were prepared from the cultured S. crispa by repeated extraction with hot water (SCHWE), cold NaOH (SCCA), and then hot NaOH (SCHA). HWE was further separated by 1 volume (SCHWE1v) or 4 volumes (SCHWE4v) of ethanol-precipitable fractions. By chemical, enzymic, and NMR analyses, the primary structures of SCHWE1v, SCCA, and SCHA were 6-branched 1,3-beta-glucan, having one branch in approximately every third mainchain unit. All of these fractions showed antitumor activity to the solid form of Sarcoma 180 in ICR mice with strong vascular dilation and hemorrhage reaction. These fractions also showed enhanced hematopoietic response to cyclophosphamide induced leukopenic mice following intraperitoneal or peroral administration.
Mashiba H, Matsunaga K. **Inhibition and augmentation of lymphoma metastasis by adoptively transferred peritoneal macrophages in hamster.** Cancer Lett. 1986 Oct;33(1):11-8. PMID: 3768859 [PubMed - indexed for MEDLINE]	The effect of adoptively transferred peritoneal exudate cells on the metastasis of hamster lymphoma was studied. Metastatic spread occurring after the surgical removal of a primary tumor was considerably inhibited by the adoptive transfer of the peritoneal exudate cells (PEC) stimulated by immunostimulants, using a streptococcal preparation (OK-432) or a purified beta (1-3) glucan (SPG). However, the inhibitory effect on metastasis was abrogated by the in vitro treatment of the peritoneal adherent cells with silica. PEC stimulated with lymphokines in vitro was also effective in inhibiting metastasis. However, the adoptive transfer of peritoneal adherent cells treated in vitro with 12-O-tetradecanoylphorbol acetate (TPA) in vitro, augmented metastatic spread in tumor-bearing hamsters which usually exhibit concomitant immunity. The relation of the state of the functional activity of macrophages to metastasis is discussed.
Bobek P, Galbavy S. **Effect of pleuran (beta-glucan from Pleurotus ostreatus) on the antioxidant status of the organism and on dimethylhydrazine-induced precancerous lesions in rat colon.** Br J Biomed Sci. 2001;58(3):164-8. PMID: 11575739 [PubMed - indexed for MEDLINE]	The effect of pleuran (beta-1,3-D-glucan isolated from the oyster mushroom Pleurotus ostreatus) on the antioxidant status of the organism and on the development of precancerous aberrant crypt foci (ACF) lesions in the colon is studied in the male Wistar rat. A diet containing either 10% pleuran or 10% cellulose was compared with a cellulose-free diet and both were found to significantly reduced conjugated diene content in erythrocytes and in liver. Particularly significant was the reduction of conjugated dienes in the colon following pleuran administration. Diets containing cellulose and pleuran reduced glutathione peroxidase (GSH-PX) activity and increased catalase activity in erythrocytes. Pleuran increased superoxide dismutase (SOD) and GSH-PX activity (compared with the cellulose diet), and glutathione reductase activity (compared with the cellulose-free diet) in liver; and both diets reduced glutathione levels significantly in the colon. ACF lesions developed in the colon of all animals fed a cellulose-free diet; however, the incidence was reduced to 64% and 60% following the cellulose and pleuran diets, respectively. The highest average count of the most frequent small ACF lesions--and highest total count--was seen in animals fed a cellulose-free diet. Although ACF lesions were reduced by the cellulose diet, the more significant reduction statistically (>50%) was achieved with the pleuran diet.

Takeyama T, Suzuki I, Ohno N, Oikawa S, Sato K, Ohsawa M, Yadomae T. **Distribution of grifolan NMF-5N (I/B), a chemically modified antitumor beta-glucan in mice.** J Pharmacobiodyn. 1988 Jun;11(6): 381-5. PMID: 3171879 [PubMed - indexed for MEDLINE]	The distribution of a 3H-labeled chemically modified antitumor beta-glucan, grifolan NMF-5N (I/B), in various tissues after an injection into mice was examined in order to obtain information on distribution of the parent antitumor beta-glucan, grifolan NMF-5N. Grifolan NMF-5N was treated with sodium metaperiodate and sodium borotritide to obtain tritium-labeled grifolan NMF-5N [3H-grifolan (I/B)]. When 3H-grifolan (I/B) was administered into normal mice by intraperitoneal (i.p.) or intravenous (i.v.) injection, radioactivity was detected in various mouse tissues. Next, 3H-grifolan (I/B) was injected into tumor-bearing mice 7 d after the tumor inoculation, which is the most effective administration timing for the antitumor effect of grifolan NMF-5N. The results indicated a strong radioactivity in spleens and tumor masses. These results suggested a close relationship between the antitumor activity and the distribution of grifolan NMF-5N in mice.
Takeyama T, Suzuki I, Ohno N, Oikawa S, Sato K, Ohsawa M, Yadomae T. **Host-mediated antitumor effect of grifolan NMF-5N, a polysaccharide obtained from Grifola frondosa.** J Pharmacobiodyn. 1987 Nov;10(11):644-51. PMID: 3446772 [PubMed - indexed for MEDLINE]	The antitumor mechanism of grifolan NMF-5N, a beta-1,3-glucan obtained from mycelia of Grifola frondosa, was examined. Grifolan NMF-5N did not show direct cytocidal effect on cultured tumor cells. However, intraperitoneal injection of grifolan NMF-5N increased the number of peritoneal exudate cells and peritoneal adherent cells which showed cytostatic activity towards syngeneic tumor cells. In an in vivo assay, the administration of carrageenan, an inhibitor of macrophage function, reduced the antitumor activity of grifolan NMF-5N. The delayed-type hypersensitivity reaction was augmented in the grifolan NMF-5N-administered mice. The administration of NMF-5N augmented the induction of cytotoxic T cells but the antitumor activity of grifolan NMF-5N was reduced in athymic nu/nu mice. In addition, the treatment with anti-Thy 1,2 antibody and complement C' of spleen cells taken from mice which showed regression of tumor due to grifolan NMF-5N, reduced the neutralizing effect in Winn assay. These results suggested that grifolan NMF-5N shows antitumor activity via host-mediated mechanisms and both macrophages and T cells play important roles in the mechanisms.
Suzuki I, Takeyama T, Ohno N, Oikawa S, Sato K, Suzuki Y, Yadomae T. **Antitumor effect of polysaccharide grifolan NMF-5N on syngeneic tumor in mice.** J Pharmacobiodyn. 1987 Feb;10(2):72-7. PMID: 3598845 [PubMed - indexed for MEDLINE]	Antitumor activity of grifolan NMF-5N, a beta-1,3-glucan obtained from mycelia of Grifola frondosa, was examined. Grifolan NMF-5N showed antitumor activities in allogeneic and syngeneic murine tumor systems. In the allogeneic tumor system, a potent antitumor activity over 95% was observed against the solid form of sarcoma 180 when grifolan NMF-5N was injected intraperitoneally (i.p.) at 25-200 micrograms/mouse daily for 10 successive days. In the syngeneic tumor systems, significant antitumor activities were observed against Meth A fibrosarcoma and MM 46 carcinoma by injection at 100 micrograms/mouse daily for 5 successive days, especially i.p. injection at day 7-11, when the tumor cells were inoculated subcutaneously (s.c.) on day 0. Moreover, when grifolan NMF-5N was injected i.p. every other week, significant antitumor activity was also observed. In addition, a single treatment with grifolan NMF-5N at 500 micrograms/mouse showed antitumor activities. Grifolan NMF-5N exhibited antitumor activities against these two syngeneic tumors by intraveneous (i.v.) injection. However, a marked inhibitory activity was observed by intratumorous (i.t.) injection against Meth A fibrosarcoma but not against MM46 carcinoma. These results suggest that antitumor activities of grifolan NMF-5N in murine syngeneic tumor systems depend on not only dosage but also injection routes and timing.

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Ohno N, Adachi Y, Suzuki I, Oikawa S, Sato K, Ohsawa M, Yadomae T. **Antitumor activity of a beta-1,3-glucan obtained from liquid cultured mycelium of Grifola frondosa.** J Pharmacobiodyn. 1986 Oct;9(10): 861-4. PMID: 3820062 [PubMed - indexed for MEDLINE]	The antitumor activity of a branched beta-1,3-glucan "grifolan LE" purified from liquid cultures of Grifola frondosa (Ohno et al. Chem. Pharm. Bull., 34, 1709-1715 (1986] was examined on an allogeneic murine tumor system. By intraperitoneal (i.p.) administration (100-200 micrograms/mouse/d X 5) at days 1 to 9 from the tumor transplantation, grifolan LE showed marked inhibitory activity on the growth of solid form sarcoma 180 in ICR mice. Significant activity was also observed in intravenous (i.v.) or intratumoral (i.t.) administrations. However, the oral (p.o.) administration of grifolan LE was not effective. I.p. administration of grifolan LE at a dose of 100 micrograms/mouse/d X 5 before the tumor transplantation showed significant inhibition of tumor growth. I.p. administration of grifolan LE at day +11 to +19 was also effective. Grifolan LE was not effective on the ascites form of sarcoma 180. The pretreatment of sarcoma 180 cell with grifolan LE in vitro did not affect tumor growth. The mice cured from the solid form of sarcoma 180 by administration of grifolan LE had the ability to reject the same tumor cell. From these results, it is suggested that the antitumor activity of grifolan LE occurred by modification of biological responses.
Kunimoto T, Baba H, Nitta K. **Antitumor polysaccharide-induced tumor-regressing factor in the serum of tumor-bearing mice: purification and characterization.** J Biol Response Mod. 1986 Jun;5(3):225-35. PMID: 3723139 [PubMed - indexed for MEDLINE]	Marked tumor-regressing activity was induced in the serum of S180 tumor-bearing mice by injection of an antitumor polysaccharide, CM-TAK [carboxymethylated beta(1-3)glucan]. Maximal activity was induced 7-14 days after the tumor transplantation and 10-12 h after CM-TAK treatment. A quantitative assay for the activity was established on the basis of the initial decrease in the number of the tumor cells within 24 h. The factor with tumor-regressing activity was purified 10,000-fold by the series of hydroxylapatite chromatography, ammonium sulfate precipitation, anion-exchange chromatography, gel filtration, and boronate-mediated affinity chromatography. The molecular weight was estimated to be 250,000 by gel filtration. The activity was proteinase K sensitive, but relatively resistant to trypsin. Neuraminidase did not affect the activity. It is believed that the tumor-regressing factor is different from the tumor necrosis factor.
Borchers AT, Stern JS, Hackman RM, Keen CL, Gershwin ME. **Mushrooms, tumors, and immunity.** Proc Soc Exp Biol Med. 1999 Sep;221(4):281-93. Review. PMID: 10460691 [PubMed - indexed for MEDLINE]	Medicinal properties have been attributed to mushrooms for thousands of years. Mushroom extracts are widely sold as nutritional supplements and touted as beneficial for health. Yet, there has not been a critical review attempting to integrate their nutraceutical potential with basic science. Relatively few studies are available on the biologic effects of mushroom consumption, and those have been performed exclusively in murine models. In this paper, we review existing data on the mechanism of whole mushrooms and isolated mushroom compounds, in particular (1-->3)-beta-D-glucans, and the means by which they modulate the immune system and potentially exert tumor-inhibitory effects. We believe that the antitumor mechanisms of several species of whole mushrooms as well as of polysaccharides isolated from Lentinus edodes, Schizophyllum commune, Grifola frondosa, and Sclerotinia sclerotiorum are mediated largely by T cells and macrophages. Despite the structural and functional similarities of these glucans, they differ in their effectiveness against specific tumors and in their ability to elicit various cellular responses, particularly cytokine expression and production. Unfortunately, our data base on the involvement of these important mediators is still rather limited, as are studies concerning the molecular mechanisms of the interactions of glucans with their target cells. As long as it remains unclear what receptors are involved in, and what downstream events are triggered by, the binding of these glucans to their target cells, it will be difficult to make further progress in understanding not only their antitumor mechanisms but also their other biological activities.

Beta 1,3-Glucan Cancer Research

Abe Y, Asano T, Isono K. **The effect of free radicals from non-parenchymal cells (NPC) of the liver on the development of liver metastases in rat.** Nippon Geka Gakkai Zasshi. 1993 Oct;94(10):1092-9. Japanese. PMID: 8232183 [PubMed - indexed for MEDLINE]	Tumor cells (AH130 hepatoma cell originated from rat) were injected intraportally into Donryu rats to produce liver metastases 21 days later. Phagocyte cells activity was depressed by the administration of Silica, which significantly increased the number of surface liver metastases. Phagocyte cells were stimulated by beta 1-3-glucan, which significantly reduced the number of metastases. And the administration of free radical scavenger (SOD, Catalase) increased the number of metastases. Non parenchymal cells (NPC) of the liver play a main role of self defence line for portally liver metastases. Then free radical from these cells were noticed in this study. NPC were isolated, from pronase perfused rat liver. O2- production by activated NPC was measured by chemiluminescence with CLA. NPC activated by beta 1-3-glucan added sera increased the luminescence of CLA, and SOD depressed the production of chemiluminescence. SOD activity of hepatocytes and tumor cells (AH130) were measured by NBT methods. Hepatocytes had high potential production of SOD, in contrast AH130 had poor production. These results suggest that free radicals from liver NPC was important for protecting liver metastases.
Yoshioka Y, Uehara N, Saito H. **Conformation-dependent change in antitumor activity of linear and branched (1----3)-beta-D-glucans on the basis of conformational elucidation by carbon-13 nuclear magnetic resonance spectroscopy.** Chem Pharm Bull (Tokyo). 1992 May;40(5):1221-6. PMID: 1394638 [PubMed - indexed for MEDLINE]	The antitumor activity of (1----3)-beta-D-glucans was tested in order to clarify its conformation-dependent response together with conformational elucidation by carbon-13 nuclear magnetic resonance (13C-NMR) spectroscopy. It was shown that the following three conformations, single chain, single helix and triple helix, are readily distinguished by the high-resolution solid-state 13C-NMR method. It turned out that preparations of linear (1----3)-beta-D-glucans of a triple helical conformation were ineffective in the inhibition of tumor growth. These linear (1----3)-beta-D-glucans were converted to an effective form in the inhibition of tumor growth when they were lyophilized from dimethyl sulfoxide (DMSO) solutions as a result of a conformational change from the triple helical to the single chain forms. They were not effective, however, when assayed in DMSO solution. In contrast, it was found that a branched (1----3)-beta-D-glucan is effective not only in either saline solutions of the triple helical sample or the lyophilized sample from DMSO, but also in DMSO solution. The aforementioned drastic change in antitumor activity was interpreted in terms of resulting conformational changes as analyzed by the 13C-NMR method.
Shirasugi N, Misaki A. **Isolation, characterization, and antitumor activities of the cell wall polysaccharides from Elsinoe leucospila.** Biosci Biotechnol Biochem. 1992 Jan;56(1):29-33. PMID: 1368133 [PubMed - indexed for MEDLINE]	A cell-wall preparation from the cells of Elsinoe leucospila, which produces elsinan extracellularly when grown on sucrose or glucose-potato extract medium, was fractionated systematically. The heteropolysaccharide that was released by treatment with Actinase E digestion, comprised D-mannose, D-galactose, and D-glucose (molar ratio, 1.5:1.0:0.1). Methylation, mild acid hydrolysis, and 13C-NMR studies suggested that the polysaccharide contains a backbone of alpha-(1----6)-linked D-mannose residues having two kinds of side chains, one attached at the O-4 with single or short beta-(1----6)-linked D-galactofuranosyl residues, and the other attached at O-2 with short side chains, most probably, of alpha-(1----3)-linked D-mannopyranosyl residues. A moderately branched D-glucan fraction, obtained from the cold alkali extract, was fractionated to give an antitumor-active purified beta-(1----3)-glucan having branches of single beta-D-glucosyl groups, one out of eight D-glucose residues being substituted at the O-6.

Saito H, Yoshioka Y, Uehara N, Aketagawa J, Tanaka S, Shibata Y. **Relationship between conformation and biological response for (1----3)-beta-D-glucans in the activation of coagulation factor G from limulus amebocyte lysate and host-mediated antitumor activity. Demonstration of single-helix conformation as a stimulant.** Carbohydr Res. 1991 Sep 18;217:181-90. PMID: 1797400 [PubMed - indexed for MEDLINE]	The relationship between the conformation of (1----3)-beta-D-glucans in gel or hydrated form and the stimulation of two types of biological responses, namely, activation of coagulation Factor G from limulus amebocyte lysate (LAL) and host-mediated antitumor activity was examined. Both types were activated by the single-helical conformation, as revealed by high-resolution, solid-state 13C-n.m.r. spectroscopy. The potency of activation of Factor G was increased over 100-fold by treatment with a NaOH solution which leads to a complete or partial conversion from the triple to the single helix. Such a single-helix specific response was also demonstrated for the antitumor activity of curdlan, although the distinction was less pronounced for branched (1----3)-beta-D-glucans. The presence of the single-helix conformation was observed in schizophyllan gel, even though the triple helix is the most stable form of branched glucans in aqueous media.
Kunimoto T, Baba H, Nitta K. **Tumor-regressing factor induced by antitumor polysaccharide in the serum of tumor-bearing mice.** Hum Cell. 1990 Jun;3(2):124-30. Japanese. PMID: 2085476 [PubMed - indexed for MEDLINE]	A potent tumor-regressing activity was found in the serum of mice with S180 tumor undergoing rapid regression caused by antitumor polysaccharides. Beta (1-3) glucan including CM-TAK and lentinan and mannoglucan MGA induced such activity. It causes a rapid decrease in the number of tumor cells accompanied with a marked increase in neutrophiles in solid tumors. The entity of the activity was named as tumor-regressing factor (TRF) and was partially purified revealing a proteinaceous nature with an approximate molecular weight of 250,000. The factor was induced in a serum of tumor-bearing mice in various host-tumor combinations after the tumor growth had been established but only weakly in normal mice. The sensitivity of tumors to the factor was also dependent on the stage of tumor growth. The serum of normal mice or tumor-bearing mice without polysaccharide treatment exhibited similar activity as TRF after definite chromatographic step. The chromatographic behavior of the revealed activity was closely similar to that of the induced factor. It was postulated that a TRF-like activity exists in normal serum in a inactivated form being bound by antagonist(s) and the appropriate chromatography might remove the antagonist resulting in the active form of the factor. The concept was confirmed by reconstituting the chromatographic fractions, the revealed activity was again obscured after mixing with a certain fraction.

Morikawa K, Kikuchi Y, Abe S, Yamazaki M, Mizuno D. **Early cellular responses in the peritoneal cavity of mice to antitumor immunomodulators.** Gann. 1984 Apr;75(4):370-8. PMID: 6735035 [PubMed - indexed for MEDLINE]	The early cellular responses to antitumor immunomodulators and conventional inducers, especially the polymorphonuclear leukocyte (PMN) responses, were examined in the peritoneal cavity of mice to investigate their effect on primary defense mechanisms. Immunomodulators were classified into 5 groups in terms of PMN response on the basis of its duration (declining or persistent) and extent (high or low induction): 1) TAK (beta-1,3-glucan)-type (high, persistent), 2) lentinan-type (high, declining), 3) yeast mannan-type (low, declining), 4) LPS (lipopolysaccharide)-type (low, persistent), 5) others (no effect). Since the general PMN response is of the declining type, the persistence of PMN with TAK- and LPS-type immunomodulators is a characteristic of the PMN-inducing activity. With respect to the extent, TAK- and lentinan-type immunomodulators induced larger numbers of PMN and macrophages than conventional inducers. These results suggest that some types of immunomodulators have effects on the early host-defense mechanism. From the viewpoint of the general self-defense mechanism we also compared these PMN responses with those to bacteria and to tumor inoculation, and the properties of substances inducing high PMN response, i.e., those with the quality of "foreignness," are discussed.

Glucan Source: Lentinan	
Citation	Abstract
Ebina T. **Intratumoral administration of biological preparations-recommendation for integrative medicine.** Gan To Kagaku Ryoho. 2001 Oct;28(11):1515-8. Japanese. PMID: 11707968 [PubMed - indexed for MEDLINE]	The antitumor effect of biological preparations was examined in a double grafted tumor system. PSK is a hot water extract of cultured mycelia from Coliolus versicolor. Its protein content is about 38% and the main glycoside portion of PSK is beta-D-glucan. Lentinan is purified from fruit bodies of Lentinus edodes and is a beta-1, 3-glucan. Cepharanthin is an extract from the root of Stephania cepharantha HAYATA, consisting of 4 kinds of biscoclaurine alkaloids. TAHEEBO tea is a hot water extract of Tabebuia avellanedae, the active ingredient of which is naphthoquinones. If protein-bound polysaccharides were to be used in Western medicine, these polysaccharides would be purified, but purified beta-glucan loses its beneficial effects. Similarly, when raw Cepharanthin is purified to isolate its active ingredient (an alkaloid cepharanthine), its anti-tumor effect is weakened. Clear IAP induction was observed in serum of mice treated with extracts of Coliolus versicolor and Stephania cepharantha. However, IAP induction was not observed in the serum of mice treated with purified beta-glucan or purified alkaloid. This suggests that macrophages may recognize extracts but not purified substances. In Western medicine, purified substances with known chemical structures are recognized as drugs, but overdoses of these drugs are toxic to the body, thus adverse reactions are always an issue. In Chinese medicine, mixtures containing several crude drugs are recognized as drugs, whose active ingredients are not identified. In integrative medicine, drugs are extracts that contain active ingredients with known structures and functions. We propose a Japanese version of integrative medicine which is neither Western nor Chinese.

Suzuki M, Kikuchi T, Takatsuki F, Hamuro J. **Curative effects of combination therapy with lentinan and interleukin-2 against established murine tumors, and the role of CD8-positive T cells.** Cancer Immunol Immunother. 1994 Jan;38(1):1-8. PMID: 8299113 [PubMed - indexed for MEDLINE]	The antitumor activity of a combination of an antitumor polysaccharide, lentinan (a beta 1-3 glucan with beta 1-6 branches), and interleukin-2 (IL-2) was evaluated against established MBL-2 lymphoma and S908.D2 sarcoma at i.d. sites. Treatment of the MBL-2-tumor-bearing BDF1 mice with lentinan and IL-2 induced complete regression of tumor in 87.5% of mice treated. In contrast, treatments using either lentinan or IL-2 alone failed to induce complete regression of tumor, although temporal growth inhibition of tumor was observed about in half of the mice treated. Improvements of antitumor effects by the combination of lentinan and IL-2 were also observed in the MBL-2/B6 and S908.D2/B10.D2 systems. Expression of the antitumor effects of lentinan/IL-2 treatments required the intact T cell compartment, because the effects were not observed when nude mice were used. In the MBL-2/B6 system, the antitumor action of lentinan/IL-2 treatment was abolished in mice treated with antibody to CD8 antigen, whereas antibodies to CD4 or NK1.1 were ineffective. Furthermore, augmented tumor-specific cytotoxic T lymphocyte (CTL) activity was observed in regional lymph node cells of the mice after lentinan and IL-2 administration. These data indicate that the antitumor effects of lentinan/IL-2 are mediated by CD8+ CTL but not by CD4+ T cells or NK1.1+ NK/LAK cells, and suggest that this combined therapy may be effective against even established tumors that are resistant to IL-2 therapy.
Suzuki M, Higuchi S, Taki Y, Taki S, Miwa K, Hamuro J. **Induction of endogenous lymphokine-activated killer activity by combined administration of lentinan and interleukin 2.** Int J Immunopharmacol. 1990;12(6): 613-23. PMID: 2272726 [PubMed - indexed for MEDLINE]	Lymphokine-activated killer activity in vivo (endogenous LAK activity) was found to be augmented by combined administration of lentinan, a beta (1-3) glucan with beta-1,6 branches, and interleukin 2 (IL-2). In contrast, addition of lentinan during culture in vitro did not augment LAK activity induced by IL-2. Surface marker analysis of endogenous LAK cells revealed that endogenous LAK cells induced by a combined administration of lentinan and IL-2 were all NK-type LAK cells, which express asialo-GM1 and lack T3, Thy-1 and Lyt2, whereas LAK cells generated in vitro were composed of both NK-type LAK and T-type LAK cells, which express T3 and Thy-1, and lack asialo-GM1. Furthermore, combined administration of lentinan and IL-2 was found to augment the endogenous LAK activity even in the tumor bearer, and show a substantial inhibition of tumor growth and a significant increase in survival rate in the C3H/HeN/MM46 system. Results of the present investigation offer a possible clinical application of a combination of lentinan and IL-2 for immunotherapy against cancer without detrimental sideeffects.
Baba H, Kunimoto T, Nitta K, Sato K, Hashimoto S, Kohno M, Kita Y, Ogawa H. **Rapid tumor regression and induction of tumor-regressing activity in serum by various immune-modulating agents.** Int J Immunopharmacol. 1986;8(6): 569-72. PMID: 3793324 [PubMed - indexed for MEDLINE]	A rapid decrease in the number of tumor cells from S180 tumors was caused by several antitumor polysaccharides including the beta (1-3)glucans lentinan and TAK-N and a mannoglucan MGA, but not by those lacking antitumor activity. MGA was demonstrated to induce potent tumor-regressing activity in the serum of tumor-bearing mice similar to that reported previously to be induced after an injection of CM-TAK, a carboxymethylated beta (1-3)glucan. It is probable that the induction of rapid regression of established tumors is a phenomenon common to antitumor polysaccharides and some microbiological products and that the tumor-regressing factor in the serum underlies a common mechanism.

Beta 1,3-Glucan Cancer Research

Herlyn D, Kaneko Y, Powe J, Aoki T, Koprowski H. **Monoclonal antibody-dependent murine macrophage-mediated cytotoxicity against human tumors is stimulated by lentinan.** Jpn J Cancer Res. 1985 Jan;76(1):37-42. PMID: 3918909 [PubMed - indexed for MEDLINE]	The beta (1----3) glucan lentinan was tested for its capacity to increase the cytotoxic effect of murine peritoneal macrophages for human tumor cells in the presence of monoclonal antibodies (MAbs). Activity was maximum in macrophages obtained on day 5 following intraperitoneal injection of CBA mice with 2.5 mg of lentinan per kg body weight. Macrophages stimulated by lentinan were cytotoxic in conjunction with IgG1, IgG2a and IgG3 MAbs, but not with IgG2b, IgM, or IgA MAbs. The demonstration of a similar enhancing effect by lentinan on human macrophages might have implications for potentiating the tumoricidal effect of these macrophages in the presence of tumor antigen-specific MAbs.

Beta 1,3-Glucan Cancer Research

Glucan Source: Laminarin Sulfate	
Citation	Abstract
Miao HQ, Elkin M, Aingorn E, Ishai-Michaeli R, Stein CA, Vlodavsky I. **Inhibition of heparanase activity and tumor metastasis by laminarin sulfate and synthetic phosphorothioate oligodeoxynucleotides.** Int J Cancer. 1999 Oct 29;83(3):424-31. PMID: 10495437 [PubMed - indexed for MEDLINE]	Heparanase activity correlates with the metastatic potential of tumor cells. Moreover, the anti-metastatic effect of non-anti-coagulant species of heparin and certain sulfated polysaccharides was attributed to their heparanase-inhibiting activity. We investigated the effect of a chemically sulfated polysaccharide (laminarin), consisting primarily of beta-1,3 glucan (sodium laminarin), and of synthetic phosphorothioate oligodeoxynucleotides, primarily phosphorothioate homopolymer of cytidine (SdC28), on heparanase activity and tumor metastasis. Investigation of the ability of tumor cells to degrade heparan sulfate in intact extracellular matrix revealed that heparanase activity expressed by B16-BL6 mouse melanoma cells and 13762 MAT rat mammary adenocarcinoma cells was effectively inhibited by LS (50% inhibition at 0.2-1 microgram/ml), but there was no inhibition by sodium laminarin up to a concentration of 50 microgram/ml. Complete inhibition of the melanoma heparanase was obtained in the presence of 0.1 microM SdC28. A single i.p. injection of laminarin sulfate, but not of sodium laminarin, before i.v. inoculation of the melanoma or breast-carcinoma cells inhibited the extent of lung colonization by the tumor cells by 80 to 90%. Similar inhibition was exerted by 0.1 microM SdC28. At the effective concentrations, both compounds had a small effect on proliferation of the tumor cells and on growth of the primary tumors in vivo. These results further emphasize the involvement of heparanase in tumor metastasis and the potential clinical application of diverse heparanase-inhibiting molecules such as sulfated polysaccharides and synthetic polyanionic molecules. Copyright 1999 Wiley-Liss, Inc.

Glucan Source: Glucan beads	
Citation	Abstract
Seljelid R, Bogwald J, Rasmussen LT, Larm O, Hoffman J, Berge A, Ugelstad J. **In vivo activation of mouse macrophages with beta-1,3-D-glucan-derivatized plastic beads.** Scand J Immunol. 1985 Jun;21(6):601-5. PMID: 4023630 [PubMed - indexed for MEDLINE]	Macrophages obtained from animals treated with beta-1,3-D-glucan-derivatized plastic beads were greatly stimulated, as judged by morphology, esterase release, and cytostatic effect on L-929 tumour cells in vitro. The pretreatment of mice with such beads conferred an apparent absolute local resistance to an otherwise lethal pneumococcal infection but had no effect on the growth of intraperitoneal AA ascites sarcoma. Moreover, peritoneal cells from animals pretreated with glucan beads did not protect the animals in a Winn assay.

Beta 1,3-Glucan Cancer Research

Glucan Source: Fungus Sclerotinia Sclerotiorum (SSG)	
Citation	Abstract
Suda M, Ohno N, Adachi Y, Yadomae T. **Relationship between the tissue distribution and antitumor activity of highly branched (1-->3)-beta-D-glucan, SSG.** Biol Pharm Bull. 1994 Jan;17(1):131-5. PMID: 8148801 [PubMed - indexed for MEDLINE]	Distribution of 3H-labeled (1-->3)-beta-D-glucan([3H]SSG) obtained from the culture filtrate of Sclerotinia sclerotiorum IFO 9395, in various tissues in tumor-bearing mice was examined. [3H]SSG administered intra-peritoneally was mainly detected in liver, spleen, kidney and tumor masses. In contrast to i.p. administration, intra-lesionally administered [3H]SSG was not released from the tumor. Similarly, in a double grafted tumor system, [3H]SSG was located in the administered tumor and not distributed in the distant site tumor, in spite of the fact that significant antitumor effect was shown in both tumor sites in this system. Winn assay confirmed the activation of the systemic antitumor immunity. These results suggested that the distribution of glucans would be one important factor in determining their antitumor effects. However, this would not always be necessary if systemic immunity could be induced.
Sakurai T, Ohno N, Suzuki I, Yadomae T. **Effect of soluble fungal (1-->3)-beta-D-glucan obtained from Sclerotinia sclerotiorum on alveolar macrophage activation.** Immunopharmacology. 1995 Aug;30(2):157-66. PMID: 8530257 [PubMed - indexed for MEDLINE]	In this study, we examined the effect of systemic administration of SSG, a soluble highly branched (1-->3)-beta-D-glucan obtained from a fungus Sclerotinia sclerotiorum IFO 9395, on pulmonary immune responses in mice. SSG (10 mg/kg) administered intravenously (i.v.) rapidly leaked into the alveolar space and enhanced several functions of alveolar macrophages (AMs), such as phagocytic activity, lysosomal enzyme activity, active oxygen secretion and cytokine production, on day 1 post-administration. However, kinetic changes of influx of SSG into alveoli and AM activation after SSG treatment were different. The enhanced AM functions decreased to control value on day 2 when SSG still existed at the alveolar space. Additionally, a high dose (500 micrograms/ml) of SSG was needed to activate AMs in vitro. These data imply that the stimulation by SSG alone is not effective on AM activation. SSG administered i.v. also augmented interferon gamma (IFN gamma) mRNA expression in the lung tissue, and the kinetic change of the expression was similar to that of AM activation. Additionally, a synergistic effect of SSG and IFN gamma was observed on AM activation in vitro. It may be possible that IFN gamma produced by pulmonary T cells is one of the important factors for AM activation in vivo by SSG injection. Furthermore, SSG administered i.v. enhanced candidacidal activity and cytolytic activity against pulmonary metastatic Lewis lung carcinoma (3LL) cells of AMs, and inhibited significantly the experimental pulmonary metastasis of 3LL cells. These observations are very useful for the clinical application of SSG as a biological response modifier (BRM).

Suda M, Ohno N, Adachi Y, Yadomae T. **Modulation of the antitumor effect and tissue distribution of highly branched (1-->3)-beta-D-glucan, SSG, by carrageenan.** Biol Pharm Bull. 1995 May;18(5):772-5. PMID: 7492998 [PubMed - indexed for MEDLINE]	The action of carrageenan (CAR), a representative blocking reagent for phagocytes, on the antitumor effect and tissue distribution of highly branched (1-->3-beta-D-glucan, SSG, was examined. CAR inhibited the antitumor effect of intraperitoneally administered SSG only when applied before inoculation of the tumor, and had little effect when applied after tumor inoculation. A similar result was observed when SSG was administered intralesionally. In contrast, CAR had considerable effect on tissue distribution of i.p. SSG. The differences with respect to the results in normal mice were: 1) the distribution of SSG from the peritoneal cavity to the rest of the body was inhibited, 2) large numbers of peritoneal exudate cells (PEC) were produced and a relatively high concentration of 3H-SSG was found in the PEC fraction 48h after administration of 3H-SSG, 3) one week after administration, 3H-SSG was distributed to throughout the body but the amount of 3H-SSG distributed was lower than in normal mice, 4) a significant amount of 3H-SSG was recovered from ligaments (containing omental milky spots, peritoneum, mesentery and associated fat) in which negligible amounts were found in normal mice. The results suggest that the inhibition of the antitumor effect of SSG by CAR probably results from the prevention of the natural resistance of mice which is related to phagocytic function, and that the distribution of SSG to throughout the body is significantly modulated by CAR.
Suzuki I, Hashimoto K, Ohno N, Tanaka H, Yadomae T. **Immunomodulation by orally administered beta-glucan in mice.** Int J Immunopharmacol. 1989;11(7): 761-9. PMID: 2599714 [PubMed - indexed for MEDLINE]	Orally administered SSG, a beta-1,3-glucan obtained from the culture filtrate of the fungus Sclerotinia sclerotiorum IFO 9395, was examined for effects on immune responses in mice. The proliferative responses of spleen cells from SSG-administered mice (40 or 80 mg/kg, daily for 5 or 10 consecutive days) to a T-cell mitogen, concanavalin A (Con A), or a B-cell mitogen, lipopolysaccharide (LPS), were higher than those from normal mice. Oral administration of SSG (80 mg/kg) to mice also enhanced the activities of both natural killer (NK) cells in spleen and the lysosomal enzyme of peritoneal macrophages. Furthermore, significant inhibition of tumor growth was observed in syngeneic tumor systems when SSG was administered directly after tumor implantation. The inhibiting effect required high doses of SSG (over 80 mg/kg). These results demonstrate that SSG can potentiate the immune response of mice following oral administration.
Suzuki I, Hashimoto K, Yadomae T. **The effects of a highly branched beta-1,3-glucan, SSG, obtained from Sclerotinia sclerotiorum IFO 9395 on the growth of syngeneic tumors in mice.** J Pharmacobiodyn. 1988 Aug;11(8): 527-32. PMID: 3236210 [PubMed - indexed for MEDLINE]	The effects of a highly branched beta-1,3-glucan, SSG, obtained from a culture filtrate of a fungus, Sclerotinia sclerotiorum IFO 9395, on the growth of syngeneic tumors and antitumor effector cells were examined. In the Meth A solid tumor systems, SSG administered intraperitoneally (i.p.), intralesionally (i.l.), or intravenously (i.v.) showed significant antitumor activities.Furthermore, SSG administered i.p. also showed effective activities against IMC carcinoma. SSG enhanced nonspecific antitumor effector functions, such as natural killer activity of spleen cells and the cytolytic activity of peritoneal macrophages. Additionally, SSG increased the specific immune response (cytotoxic T lymphocyte activity) against allogeneic tumor cells.

Ohno N, Kurachi K, Yadomae T. **Antitumor activity of a highly branched (1----3)-beta-D-glucan, SSG, obtained from Sclerotinia sclerotiorum IFO 9395.** J Pharmacobiodyn. 1987 Sep;10(9): 478-86. PMID: 3437391 [PubMed - indexed for MEDLINE]	The antitumor activity of a highly branched (1----3)-beta-D-glucan, SSG, purified from the liquid culture filtrate of Sclerotinia sclerotiorum IFO 9395 and its several derivatives were treated in ICR mice bearing Sarcoma 180 cells. SSG was effective by both systemic (intraperitoneal and intravenous) and local (intratumoral) administrations on the solid form of Sarcoma 180 in ICR mice and the mice acquired resistance to subsequent inoculation of Sarcoma 180. However, SSG was not effective on the ascites form Sarcoma 180. The pretreatment of ICR mice with carrageenan suppressed the antitumor activity, suggesting the involvement of macrophages on the antitumor activity. Derivatives prepared from SSG by periodate oxidation/borohydride reduction showed antitumor activity, but those obtained after acetylation, carboxymethylation and hydroxyethylation were less active. From these results, it is suggested that SSG is a useful antitumor glucan which modifies biological responses and can be used as a source for some antitumor derivatives.

Glucan Source: Bacterial	
Citation	Abstract
Kasai S, Fujimoto S, Nitta K, Baba H, Kunimoto T. **Antitumor activity of polymorphonuclear leukocytes activated by a beta-1,3-D-glucan.** J Pharmacobiodyn. 1991 Sep;14(9): 519-25. PMID: 1779406 [PubMed - indexed for MEDLINE]	The antitumor activity of mouse polymorphonuclear leukocyte (PMN) treated with a beta-1,3-D-glucan from Alcaligenes faecalis var. myxogenes IFO 13140 (TAK-N) and its carboxymethylated derivative (CM-TAK) was investigated in vitro and in vivo. ICR mouse PMN showed strong cytotoxicity against sarcoma 180 cells and inhibition of the growth of the tumor cells in vitro in the presence of TAK-N but not in the presence of CM-TAK. Since the cytotoxicity induced by TAK-N was almost completely inhibited by catalase, it seems to be mediated by H2O2 production by PMN. On the other hand, TAK-N induced no cytotoxicity in macrophages and neither did CM-TAK in PMN or in macrophage. Intraperitoneal injection of TAK-N into ICR mice induced a large number of PMN and macrophages in the peritoneal cavity. The peritoneal exudate PMN which were harvested at 10 to 72 h after TAK-N injection showed cytotoxicity against sarcoma 180 cells, but the peritoneal exudate macrophages did not. Treatment of sarcoma 180 ascites tumor-bearing ICR mice with TAK-N at a dose of 100 mg/kg prolonged significantly the survival time over that of the control. These results indicate that TAK-N induces PMN cytotoxicity against sarcoma 180 cells not only in vitro but also in vivo. The antitumor effect of TAK-N on sarcoma 180 ascites tumor seems to be derived from PMN stimulated with TAK-N.

Beta 1,3-Glucan Cancer Research

Araki A, Inoue T, Kimura S, Fukase S, Sendo F. **Enhancement of polymorphonuclear leukocyte-mediated tumor cytotoxicity by serum factor(s).** Jpn J Cancer Res. 1990 Jan;81(1):69-78. PMID: 2108949 [PubMed - indexed for MEDLINE]	It has been reported that beta-1,3-D-glucan isolated from Alcaligenes faecalis (TAK) promoted tumor cytolysis by mouse polymorphonuclear leukocytes (PMN). We investigated the effect of serum on mouse PMN tumor cytolysis induced by TAK and other PMN stimulators. Addition of fetal calf serum (FCS) to the cytolysis assay enhanced tumor cytolysis by PMN in a dose-dependent manner. Sera obtained from horses, mice, and rats were also effective enhancers of PMN tumor cytolysis. When FCS was added after the assay was under way, the enhancing effect decreased proportionally to the time elapsed. The enhancing activity was detected over a broad range of fractions with a peak at 170 kD by fractionation on a Superose 6 column. The responsible factor(s) in serum was stable after treatment at 60 degrees C, 30 min or after lowering the pH to 2. Mouse PMN stimulated with TAK increased production of hydrogen peroxide in the presence of FCS.
Fukase S, Inoue T, Arai S, Sendo F. **Tumor cytotoxicity of polymorphonuclear leukocytes in beige mice: linkage of high responsiveness to linear beta-1,3-D-glucan with the beige gene.** Cancer Res. 1987 Sep 15;47(18):4842-7. PMID: 3621179 [PubMed - indexed for MEDLINE]	Beige mice (bg/bg) have many functional defects in their leukocytes and these phenotypes are inherited autosomal recessively. We studied the tumor cytotoxicity of polymorphonuclear leukocytes (PMN) obtained from bg/bg. The intensity of tumor cytotoxicity of PMN induced by linear beta-1,3-D-glucan was significantly higher in bg/bg PMN than in PMN of heterozygous control mice (bg/+). To analyze this phenomenon more precisely from the genetic viewpoint, we determined the tumor cytotoxicity of PMN from mice obtained by several mating experiments. (a) The intensity of linear beta-1,3-D-glucan-induced PMN cytotoxicity was found to be genetically defined and linked completely with the beige gene. In litter mates obtained from bg/+(female) X bg/bg(male), bg/bg(female) X bg/+(male), and bg/+(female) X bg/+(male) mating, PMN from only bg/bg showed significantly higher tumor cytotoxicity than those from bg/+ or mice that do not possess the beige gene (+/+). (b) The tumor cytotoxicity induced by other stimulants (phorbol myristate acetate and cytokines) was not significantly higher in bg/bg than bg/+ or +/+ PMN. It was concluded that the high responsiveness to linear beta-1,3-D-glucan in terms of tumor cytotoxicity of PMN was determined by the locus that is linked to the beige gene and is expressed autosomal recessively.

Beta 1,3-Glucan Cancer Research

Morikawa K, Kamegaya S, Yamazaki M, Mizuno D. **Hydrogen peroxide as a tumoricidal mediator of murine polymorphonuclear leukocytes induced by a linear beta-1,3-D-glucan and some other immunomodulators.** Cancer Res. 1985 Aug;45(8):3482-6. PMID: 2990672 [PubMed - indexed for MEDLINE]	Polymorphonuclear leukocytes (PMN) of mice can destroy tumor cells effectively in vitro in the presence of antitumor polysaccharide, linear beta-1, 3-D-glucan from Alcaligenes faecalis var. myxogenes IFO 13140 (TAK), and some other immunomodulators. In the present study, we investigated the mechanism of the tumoricidal activity of PMN induced by these immunomodulators and especially TAK. The TAK-induced PMN cytotoxicity was concluded to involve hydrogen peroxide from the following results: (a) the cytotoxicity depended on glucose consumption; (b) it was almost completely inhibited by catalase but not affected by superoxide dismutase; (c) it was not reduced by cyanide or azide, which are inhibitors of myeloperoxidase; (d) it was not affected by scavengers of singlet oxygen or hydroxyl radical; (e) release of hydrogen peroxide from PMN was observed by the addition of TAK; (f) MM46 target cells were lysed directly by hydrogen peroxide in the absence of myeloperoxidase; (g) the supernatant of PMN in the presence of TAK, tested as a stable cytotoxic factor, did not have cytotoxic activity, and protease inhibitors had no effect on this cytotoxicity. These results suggest that hydrogen peroxide is a direct cytotoxic mediator in TAK-induced PMN cytotoxicity. Next, the mechanism of PMN cytotoxicities induced by other immunomodulators was also examined and was compared with that induced by TAK. The results suggest that hydrogen peroxide is also important for these cytotoxicities whereas, unlike the results with TAK, the H2O2:halide:myeloperoxidase system may partly participate in the cytotoxicities with some immunomodulators.

Glucan Source: Aminated Glucan	
Citation	Abstract
Sveinbjornsson B, Rushfeldt C, Seljelid R, Smedsrod B. **Inhibition of establishment and growth of mouse liver metastases after treatment with interferon gamma and beta-1,3-D-glucan.** Hepatology. 1998 May;27(5):1241-8. PMID: 9581677 [PubMed - indexed for MEDLINE]	The purpose of this study was to investigate the combined antitumor effect of aminated beta-1,3-D-glucan (AG) and interferon-gamma (IFN-gamma) in an experimental liver metastasis model. Liver metastases were established by inoculation of C-26 colon carcinoma cells into the superior mesenteric vein of syngeneic mice. Treatment of mice started 24 hours after inoculation of tumor cells by daily intravenous injections of either AG, IFN-gamma, or a combination of both for a duration of 6 days. The resultant liver metastases were then quantified after an additional period of 11 days. Combination of IFN-gamma and AG inhibited the growth of liver metastases almost entirely. IFN-gamma was also very efficient, while AG alone did not exert any significant antitumor effect. These results, along with histological studies from mice receiving AG and IFN-gamma, indicated that activation and recruitment of liver macrophages may be a part of the mechanism responsible for the inhibition of metastatic growth observed in this study.

Beta 1,3-Glucan Cancer Research

Seljelid R, Figenschau Y, Bogwald J, Rasmussen LT, Austgulen R. **Evidence that tumor necrosis induced by aminated beta 1-3D polyglucose is mediated by a concerted action of local and systemic cytokines.** Scand J Immunol. 1989 Dec;30(6): 687-94. PMID: 2532395 [PubMed - indexed for MEDLINE]	Aminated beta 1-3D polyglucose (AG) causes regression of Meth A sarcoma in syngeneic mice when injected systemically on day 7 after tumour inoculation. AG does not concentrate in the tumour, but distributes throughout the body. AG treatment causes release of large amounts of interleukin 1 (IL-1) both in vivo and in macrophage cultures in vitro. AG is a weak stimulus for tumour necrosis factor (TNF) release both in vitro and in vivo. However, tumour tissue and sera from untreated mice on days 3 and 7 after inoculation contain significant amounts of TNF, whereas tumour tissue and sera on day 14 contain insignificant amounts of TNF. This correlates exactly with the sensitivity to AG treatment. IL-1, and TNF when injected locally cause reduction in tumour blood circulation and also shrinkage of the tumour. All these facts taken together indicate that the tumour circulatory failure and necrosis induced by AG are mediated by local TNF-unrelated to the treatment--potentiated by systemic cytokines triggered by the AG.
Seljelid R. **A water-soluble aminated beta 1-3D-glucan derivative causes regression of solid tumors in mice.** Biosci Rep. 1986 Sep;6(9):845-51. PMID: 3814772 [PubMed - indexed for MEDLINE]	Meth A sarcoma, when inoculated in the skin, grew progressively in hybrid CB6 F1(Balb/c X C57B1/6) mice. When water-soluble aminated beta 1-3D-glucan (AG) was injected intravenously or intraperitoneally on day 7 of tumor growth, the tumors underwent complete regression. When the injection was performed on day 3 there was regression of tumors in only about half of the cases. When the injection was performed on day 14 there was no apparent effect on tumor growth. Tumors in thymectonized animals did not appear to respond to treatment with AG on day 7. The relatively simple chemistry and low toxicity of AG, together with its solubility in biological fluids, makes it a promising tool in experimental--and possibly clinical--tumor therapy.
Seljelid R, Bogwald J, Hoffman J, Larm O. **A soluble beta-1,3-D-glucan derivative potentiates the cytostatic and cytolytic capacity of mouse peritoneal macrophages in vitro.** Immunopharmacology. 1984 Feb;7(1):69-73. PMID: 6715145 [PubMed - indexed for MEDLINE]	An aminated beta-1,3-D-glucan derivative of curdlan is reported to render macrophages cytostatic to L-929 cells and to potentiate macrophage cytotoxicity to the tumor cells in vitro.

Beta 1,3-Glucan Cancer Research