Beta 1,3-Glucan Radiation Research

Glucan Source: Yeast	
Citation	**Abstract**
Patchen ML, DiLuzio NR, Jacques P, MacVittie TJ. **Soluble polyglycans enhance recovery from cobalt-60--induced hemopoietic injury.** J Biol Response Mod. 1984 Dec;3(6):627-33. PMID: 6512563 [PubMed - indexed for MEDLINE]	Six soluble polyglycans (glucan-C, glucan-F, glucan-S, krestin, lentinan, and schizophyllan), two soluble polymannans (mannan-A and mannan-R), and one soluble polyfructan (levan) were assayed for their ability to enhance hemopoietic recovery in C3H/HeN mice when administered either 1 h before or 1 h after a 6.5-Gy dose of cobalt-60 radiation. Hemopoietic recovery was measured by the endogenous spleen colony assay and was compared with recovery in both radiation control mice and irradiated mice treated with glucan-P (a particulate polyglycan previously shown to enhance recovery from radiation-induced hemopoietic injury). Compared with radiation controls, when administered before irradiation, mannan-A, glucan-F, and glucan-S enhanced endogenous colony formation 4.2-5.1-fold (equivalent to glucan-P), and levan and schizophyllan approximately 2.7-fold. Lentinan, krestin, mannan-R, and glucan-C did not enhance hemopoietic recovery above radiation controls under these conditions. When polyglycan administration was delayed until after irradiation, endogenous colony formation was enhanced 3.0-3.9-fold by mannan-A, schizophyllan, glucan-S, krestin, and glucan-F (at least comparable with glucan-P) but not at all by mannan-R, levan, lentinan, or glucan-C.
Patchen ML, MacVittie TJ, Wathen LM. **Effects of pre- and post-irradiation glucan treatment on pluripotent stem cells, granulocyte, macrophage and erythroid progenitor cells, and hemopoietic stromal cells.** Experientia. 1984 Nov 15;40(11): 1240-4. PMID: 6500009 [PubMed - indexed for MEDLINE]	Glucan, a beta-1,3 polyglucose, was administered to mice either 1 h before or 1 h after a 650 rad exposure to cobalt-60 radiation. Compared to radiation controls, glucan-treated mice consistently exhibited a more rapid recovery of pluripotent stem cells and committed granulocyte, macrophage, and erythroid progenitor cells. This may partially explain the mechanism by which glucan also enhances survival in otherwise lethally irradiated mice.
Patchen ML, MacVittie TJ. **Stimulated hemopoiesis and enhanced survival following glucan treatment in sublethally and lethally irradiated mice.** Int J Immunopharmacol. 1985;7(6): 923-32. PMID: 4077349 [PubMed - indexed for MEDLINE]	Hemopoietic effects of the reticuloendothelial agent glucan were assayed in normal mice and in mice hemopoietically depleted by exposure to 60Co radiation. In normal mice, glucan administration increased the content of bone marrow and splenic transplantable pluripotent hemopoietic stem cells (CFU-s), committed granulocyte-macrophage progenitor cells (GM-CFC), and pure macrophage progenitor cells (M-CFC). Erythroid progenitor cells (CFU-e) were increased only in the spleen. In sublethally irradiated mice (650 rads), glucan increased the number of endogenous pluripotent hemopoietic stem cells (E-CFU) when administered either before or after irradiation. The most pronounced effects were observed when glucan was administered 1 day before, 1 h before, or 1 h after irradiation. In addition, the administration of glucan before lethal irradiation (900 rads) enhanced survival. The most significant results were seen when glucan was aministered 1 day prior to irradiation. The possibility of using agents such as glucan to enhance hemopoietic reconstitution and prevent septicemia following chemotherapy and/or radiotherapy is discussed.
Patchen ML, MacVittie TJ. **Hemopoietic effects of intravenous soluble glucan administration.** J Immunopharmacol. 1986;8(3):407-25. PMID: 3760593 [PubMed - indexed for MEDLINE]	A soluble form of the reticuloendothelial- and immune modulating agent glucan (glucan-F) has been evaluated for its effects on hemopoiesis. A single 5.0 mg intravenous injection of glucan-F into C3H/HeN mice increased peripheral white blood cellularity, bone marrow and splenic cellularity, bone marrow and splenic granulocyte-macrophage progenitor cell numbers (GM-CFC), and splenic pluripotent stem cell (CFU-s) and erythroid progenitor cell (CFU-e) numbers. Serum levels of granulocyte-macrophage colony stimulating activity (CSA) were also elevated following glucan-F administration. These hemopoietic responses correlate well with those previously shown to be induced by intravenous administration of particulate glucan (glucan-P). In contrast to glucan-P, however, intravenous glucan-F administration has been shown not to induce granuloma formation and severe hepatosplenomegaly, thus the potential clinical use of glucan-F as a hemopoietic stimulant is more likely than that of glucan-P.

Beta 1,3-Glucan Radiation Research

Patchen ML, MacVittie TJ. **Comparative effects of soluble and particulate glucans on survival in irradiated mice.** J Biol Response Mod. 1986 Feb;5(1):45-60. PMID: 3958754 [PubMed - indexed for MEDLINE]	The survival-enhancing capabilities of particulate (P) and soluble (F) glucan, a B-1,3 polyglycan biological response modifier, were assayed in 60Co irradiated mice. Although glucan-P was slightly more effective than glucan-F, both glucans significantly enhanced survival in otherwise lethally irradiated (9.0-11.0 Gy) C3H/HeN mice. Following 9.0 Gy, 60% of the glucan-P treated and 53% of the glucan-F treated mice exhibited long-term survival as opposed to 0% of the radiation control mice. The survival-enhancing effects of glucan-P and glucan-F decreased as the radiation dose increased to 11.0 Gy. At higher radiation doses (e.g., 12.0 Gy) neither glucan preparation was capable of enhancing survival. Both glucan-P and glucan-F enhanced the recovery of peripheral blood white cell numbers, platelet numbers, and hematocrit values. In addition, both agents increased endogenous pluripotent hemopoietic stem cell numbers in sublethally irradiated mice. Taken together, these results demonstrate that both glucan-P and glucan-F can significantly enhance survival in lethally irradiated mice. However, these agents appear to function specifically by enhancing hemopoietic recovery and are not effective at radiation does also known to induce gastrointestinal damage.
Patchen ML, MacVittie TJ, Brook I. **Glucan-induced hemopoietic and immune stimulation: therapeutic effects in sublethally and lethally irradiated mice.** Methods Find Exp Clin Pharmacol. 1986 Mar;8(3):151-5. PMID: 3713378 [PubMed - indexed for MEDLINE]	The hemopoietic effects of glucan, a beta 1,3 polyglycan biological response modifier, were assayed in normal and irradiated mice. In normal mice, glucan administration increased the content of bone marrow and splenic transplantable pluripotent hemopoietic stem cells (CFU-s), committed granulocyte-macrophage progenitor cells (GM-CFC), and pure macrophage progenitor cells (M-CFC). In mice partially hemopoietic depleted by exposure to .48r3 p000tw[n]ormal mvival-ee gin 60% of lls

Beta 1,3-Glucan Radiation Research

Patchen ML, Chirigos MA, Brook I. **Use of glucan and other immunopharmacological agents in the prevention and treatment of acute radiation injuries.** Fundam Appl Toxicol. 1988 Nov;11(4):573-4. No abstract available. PMID: 3229582 [PubMed - indexed for MEDLINE]	N/A
Patchen ML, MacVittie TJ, Jackson WE. **Postirradiation glucan administration enhances the radioprotective effects of WR-2721.** Radiat Res. 1989 Jan;117(1):59-69. PMID: 2536480 [PubMed - indexed for MEDLINE]	Based on murine survival studies, endogenous hemopoietic spleen colony formation (E-CFU), and recovery of bone marrow and splenic granulocyte-macrophage colony-forming cells (GM-CFC), it was demonstrated that the postirradiation administration of glucan, an immunomodulator and hemopoietic stimulant, enhances the radioprotective effects of WR-2721. LD50/30 dose reduction factors for mice treated with WR-2721 (200 mg/kg approximately 30 min before irradiation), glucan (250 mg/kg approximately 1 h after irradiation), or both agents were 1.37, 1.08, and 1.52, respectively. Enhanced survival in mice treated with both agents appeared to be due in part to glucan's ability to accelerate hemopoietic regeneration from stem cells initially protected from radiation-induced lethality by WR-2721. Following a 10-Gy radiation exposure, E-CFU numbers in mice treated with saline, WR-2721, glucan, or both WR-2721 and glucan were 0.05 +/- 0.03, 6.70 +/- 1.05, 0.95 +/- 0.24, and 33.90 +/- 2.96, respectively. Similarly, bone marrow and splenic GM-CFC numbers were greater in mice treated with both WR-2721 and glucan than in mice treated with either agent alone. These results demonstrated at least additive radioprotective effects when mice were given WR-2721 prior to irradiation and glucan following irradiation. These effects appeared to depend on the sequential cell protection mediated by WR-2721 and hemopoietic repopulation mediated by glucan.
Patchen ML, MacVittie TJ, Weiss JF. **Combined modality radioprotection: the use of glucan and selenium with WR-2721.** Int J Radiat Oncol Biol Phys. 1990 May;18(5):1069-75. PMID: 2161407 [PubMed - indexed for MEDLINE]	Glucan, WR-2721, and selenium, three agents with distinct radioprotective mechanisms, were evaluated in C3H/HeN mice for survival-enhancing and hemopoietic-regenerating effects when administered alone or in combinations before exposure to 60Co radiation. At LD50/30 radiation doses (radiation doses lethal for 50% of mice within 30 days postexposure), dose reduction factors of 1.21, 1.02, 1.37, 1.51, and 1.66 were obtained following glucan (75 mg/kg i.v., -20 hr), selenium (0.8 mg/kg, i.p., -20 hr), WR-2721 (200 mg/kg, i.p., -30 min), glucan + WR-2721, and glucan + selenium + WR-2721 treatments, respectively. All treatments increased numbers of hemopoietic stem cells as measured by the day 12 endogenous spleen colony-forming unit (E-CFU) assay; the most significant E-CFU effects, however, were observed following glucan + WR-2721 and glucan + selenium + WR-2721 treatments. Combined modality treatments were also more effective than single-agent treatments at accelerating bone marrow and splenic granulocyte-macrophage colony-forming cell (GM-CFC) regeneration. These results demonstrate the value of multiple-agent radioprotectants. PMID: 2161407 [PubMed - indexed for MEDLINE]

Beta 1,3-Glucan Radiation Research

Patchen ML, MacVittie TJ, Solberg BD, Souza LM. **Survival enhancement and hemopoietic regeneration following radiation exposure: therapeutic approach using glucan and granulocyte colony-stimulating factor.** Exp Hematol. 1990 Oct;18(9):1042-8. PMID: 1697806 [PubMed - indexed for MEDLINE]	C3H/HeN female mice were exposed to wholebody cobalt-60 radiation and administered soluble glucan (5 mg i.v. at 1 h following exposure), recombinant human granulocyte colony-stimulating factor (G-CSF; 2.5 micrograms/day s.c., days 3-12 following exposure), or both agents. Treatments were evaluated for their ability to enhance hemopoietic regeneration, and to increase survival after radiation-induced myelosuppression. Both glucan and G-CSF enhanced hemopoietic regeneration alone; however, greater effects were observed in mice receiving both agents. For example, on day 17 following a sublethal 6.5-Gy radiation exposure, mice treated with saline, G-CSF, glucan, or both agents, respectively, exhibited 36%, 65%, 50%, and 78% of normal bone marrow cellularity, and 84%, 175%, 152%, and 212% of normal splenic cellularity. At this same time, granulocyte-macrophage colony-forming cell (GM-CFC) values in saline, G-CSF, glucan, or combination-treated mice, respectively, were 9%, 46%, 26%, and 57% of normal bone marrow values, and 57%, 937%, 364%, and 1477% of normal splenic values. Endogenous spleen colony formation was also increased in all treatment groups, with combination-treated mice exhibiting the greatest effects. Likewise, although both glucan and G-CSF alone enhanced survival following an 8-Gy radiation exposure, greatest survival was observed in mice treated with both agents. These studies suggest that glucan, a macrophage activator, can synergize with G-CSF to further accelerate hemopoietic regeneration and increase survival following radiation-induced myelosuppression.
Baker WH, Nold JB, Patchen ML, Jackson WE. **Histopathologic effects of soluble glucan and WR-2721, independently and combined in C3H/HeN mice.** Proc Soc Exp Biol Med. 1992 Nov;201(2):180-91. PMID: 1329111 [PubMed - indexed for MEDLINE]	Soluble glucan, an immunomodulator, and Walter Reed (WR)-2721, a radioprotectant, increase postirradiation survival when administered before and after exposure, respectively. Combined, these agents act synergistically through WR-2721's ability to spare hematopoietic stem/progenitor cells from radiation injury and glucan's ability to subsequently stimulate spared cells to proliferate. In this study, the histopathologic effects of WR-2721 (200 mg/kg, ip) and glucan (250 mg/kg, iv), at doses capable of increasing survival in lethally irradiated mice, were evaluated in unirradiated and irradiated female C3H/HeN mice. After treatment, whole body weights and wet organ weights of liver, spleen, and kidney, as well as gross and histologic changes in these and other tissues, were monitored on Days 1, 4, 7, 11, 15, 21, and 28. Morphometric studies of splenic white and red pulps were also performed. Soluble glucan, with or without WR-2721, in unirradiated groups, was associated with splenomegaly, transient morphometrically determined perturbations of white and red pulp areas, and histologic alterations of white pulp. In irradiated mice, splenic weight loss was initially dampened in glucan groups and accompanied by morphologic and histologic changes similar to those seen in unirradiated counterparts. The subsequent rebound of splenic parameters in irradiated mice was limited to WR-2721-treated mice and was associated with hematopoietic reconstitution. Glucan, with or without WR-2721, in unirradiated groups was associated with transient hepatomegaly and associated histologic changes. Similar changes in irradiated animals were seen only in the combined treatment group.
Patchen ML, MacVittie TJ, Solberg BD, D'Alesandro MM, Brook I. **Radioprotection by polysaccharides alone and in combination with aminothiols.** Adv Space Res. 1992;12(2-3):233-48. PMID: 11537014 [PubMed - indexed for MEDLINE]	We demonstrated that glucan, a beta-1,3 polysaccharide immunomodulator, enhances survival of mice when administered before radiation exposure. Glucan's prophylactic survival-enhancing effects are mediated by several mechanisms including (1) increasing macrophage-mediated resistance to potentially lethal postirradiation opportunistic infections, (2) increasing the D(o) of hematopoietic progenitor cells, and (3) accelerating hematopoietic reconstitution. In addition, even when administered shortly after some otherwise lethal doses of radiation, glucan increases survival. Glucan's therapeutic survival-enhancing effects are also mediated through its ability to enhance macrophage function and to accelerate hematopoietic reconstitution; glucan's therapeutic potential, however, is ultimately dependent on the survival of a critical number of hematopoietic stem cells capable of responding to glucan's stimulatory effects. Preirradiation administration of the traditional aminothiol radioprotectants WR-2721 and WR-3689 has been previously demonstrated to be an extremely effective means to increase hematopoietic stem cell survival. Therapeutic glucan treatment administered in combination with preirradiation WR-2721 or WR-3689 treatment synergistically increases both hematopoietic reconstitution and survival. Such combined modality treatments offer new promise in treating acute radiation injury.

Beta 1,3-Glucan Radiation Research

Patchen ML, Brook I, Elliott TB, Jackson WE. **Adverse effects of pefloxacin in irradiated C3H/HeN mice: correction with glucan therapy.** Antimicrob Agents Chemother. 1993 Sep;37(9):1882-9. PMID: 8239601 [PubMed - indexed for MEDLINE]	Opportunistic bacterial infections are the predominant cause of death following myelosuppressive radiation exposure. When used alone, a variety of immunomodulators and antibiotics have been reported to reduce radiation-induced death. In these studies, the combined therapeutic effects of the immunomodulator glucan and the quinolone antibiotic pefloxacin were evaluated for survival-enhancing effects in myelosuppressed C3H/HeN mice. Mice were exposed to 7.9 Gy of whole-body 60Co radiation and treated with saline, glucan (250 mg/kg of body weight intravenously, 1 h after irradiation), pefloxacin (64 mg/kg/day orally, days 3 to 24 after irradiation), or glucan plus pefloxacin. Survival 30 days after irradiation in mice receiving these respective treatments was 25, 48, 7, and 85%. Evaluation of granulocyte-macrophage progenitor cell (GM-CFC) recovery in mice receiving these treatments revealed that, compared with recovery in saline-treated mice, glucan stimulated GM-CFC recovery, pefloxacin suppressed GM-CFC recovery, and glucan administered in combination with pefloxacin could override pefloxacin's hemopoietic suppressive effect.
Hofer M, Pospisil M. **Glucan as stimulator of hematopoiesis in normal and gamma-irradiated mice. A survey of the authors' results.** Int J Immunopharmacol. 1997 Sep-Oct;19(9-10):607-9. PMID: 9637361 [PubMed - indexed for MEDLINE]	Glucan, a beta-1,3-linked polyglucose derived from the yeast Saccharomyces cerevisiae, is a broad spectrum enhancer of host defense mechanisms stimulating humoral and cell-mediated immunity. On the basis of these features, glucan has been tested by the authors' research group in experiments on gamma-irradiated mice. Two glucan forms, particulate and soluble, have been studied. Attention has been focused on various application regimens in relation to the time of irradiation (pre- or postirradiation application), the possibilities of using glucan in various radiation regimens (single or repeated irradiation), combined pharmacological therapy (joint administration of glucan with cystamine or inhibitors of prostaglandin synthesis), and on the negative side effects of therapy with glucan. Some studies included also experiments on unirradiated mice. The results have demonstrated the ability of glucan to influence positively the course of the acute radiation disease. Stimulation of hematopoiesis has been found to be the most important mechanism of glucan's radioprotective effects. In this communication, the results of 11 full-length articles are summarized and discussed.

Glucan Source: Seaweed	
Citation	**Abstract**
Chertkov KS, Davydova SA, Nesterova TA, Zviagintseva TN, Eliakova LA. **Efficiency of polysaccharide translam for early treatment of acute radiation illness.** Radiats Biol Radioecol. 1999 Sep-Oct;39(5):572-7. Russian. PMID: 10576030 [PubMed - indexed for MEDLINE]	Antiradiation therapeutic efficiency of translam (1-->3; 1-->6-beta-D-glucan) produced by enzymatic synthesis out of laminarin, polysaccharide of Laminaria cychorioides, has been studied in four animal species (mice, guinea-pigs, dogs, monkeys). A stable curative effect has been observed following its administration within first 24 h after radiation exposure at doses that cause acute radiation sickness (about LD90). The preparation is nontoxic and has a broad therapeutic range which permits its practical application.

Beta 1,3-Glucan Radiation Research

Kuznetsova TA, Krylova NV, Besednova NN, Vasil'eva VN, Zviagintseva TN, Krashevskii SV, Eliakova LA. **The effect of translam on the natural resistance indices of the irradiated organism.** Radiats Biol Radioecol. 1994 Mar-Apr;34(2):236-9. Russian. PMID: 8193714 [PubMed - indexed for MEDLINE]	It has been studied the influence of translam-beta-1,3; 1,6-glucan, extracted from seaweed Laminaria, on the isolation of E. coli from spleen and on the functional activity of peritoneal macrophages of sublethal irradiated and infected mice. It has been shown the reduction of the number of microbes, isolated from spleen and stimulation of ingestive and digestive activity of macrophages following the introduction of translam in mice. This results show about the increase of natural resistance of irradiated organism under translam action and characterise this glucan as effective stimulator of immunity.
Zaporozhets TS, Besednova NN, Eliakova LA, Zviagintseva TN, Krashevskii SV. **The effect of translam on the immune response of irradiated mice.** Radiats Biol Radioecol. 1995 Mar-Apr;35(2):260-3. Russian. PMID: 7757190 [PubMed - indexed for MEDLINE]	Experimental facts about influence of new beta-1-3;1-6-glucan, extracted from seaweed Laminaria, on immune response of mice are summarized. The ability of translam to increase the number and functional activity of immunocompetent cells taking part in humoral immune response formation. The possibility of translam using for treatment and prophylaxis of radiation affections is discussed.

Glucan Source: Carboxymethylglucan (CMG)	
Citation	**Abstract**
Hofer M, Pospisil M, Bohacek J, Pipalova I, Sandula J. **Enhancement by carboxymethylglucan of early cellular damage in 1 Gy-irradiated mice.** Folia Biol (Praha). 1995;41(2):112-7. PMID: 7656994 [PubMed - indexed for MEDLINE]	Our results describe a novel carboxymethylglucan (CMG) activity, namely its radiosensitizing effect on early cellular damage in mice gamma-irradiated with a dose of 1 Gy. An increase of thymidine levels in blood plasma, determined 4 h after irradiation, was used as an indicator of the early cell death. The radiosensitizing effect was observed when administering CMG at time intervals close to irradiation time (1 h before to 1 h after irradiation). Diclofenac (an inhibitor of prostaglandin production) had no modifying effects on elevation of plasma thymidine levels induced by radiation or radiation + CMG. Pentoxifylline (an inhibitor of synthesis of tumour necrosis factor and of phosphodiesterase) administration elevated plasma thymidine to similar levels as CMG alone, combined pentoxifylline + CMG treatment had not additive effects.

Beta 1,3-Glucan Radiation Research

Pospisil M, Hofer M, Pipalova I, Viklicka S, Netikova J, Sandula J. **Enhancement of hematopoietic recovery in gamma-irradiated mice by the joint use of diclofenac, an inhibitor of prostaglandin production, and glucan, a macrophage activator.** Exp Hematol. 1992 Aug;20(7):891-5. PMID: 1628707 [PubMed - indexed for MEDLINE]	The effects of diclofenac (inhibitor of prostaglandin production) and carboxymethylglucan (immunomodulator and an agent stimulating hematopoiesis), when given to mice 1 day before gamma-irradiation, were studied. Both of the agents were administered either alone or in combination. The investigations included the assessment of post-irradiation hematopoietic recovery in terms of bone marrow and spleen cellularity and endogenous spleen colony formation, as well as the determination of the survival of lethally irradiated mice. The results demonstrated at least additive radioprotective effects when mice were given diclofenac and carboxymethylglucan in combination. Experimental evidence provided by the increased 125iodo-deoxyuridine incorporation into the spleen and elevated hydroxyurea kill of endogenous spleen colony-forming units indicated that the beneficial action of the combined treatment could be a consequence of increased cell proliferation in the hematopoietic tissue. It is likely that the inhibition of prostaglandin production (diclofenac action) and the concomitant increased release of growth factors (glucan action) shift the regulatory balance towards the predominance of positive hematopoietic control.
Pospisil M, Sandula J, Pipalova I, Hofer M, Viklicka S. **Hemopoiesis stimulating and radioprotective effects of carboxymethylglucan.** Physiol Res. 1991;40(4):377-80. PMID: 1725851 [PubMed - indexed for MEDLINE]	Carboxymethylglucan, a novel soluble derivative of beta-1,3-glucan, was found to enhance hemopoietic recovery in sublethally gamma-irradiated mice and to increase survival in lethally irradiated animals when given 24 hours prior to irradiation. Postirradiation treatment with carboxymethylglucan also induced favourable effects in terms of survival when used in combination with preirradiation cystamine administration.
Hofer M, Pospisil M, Pipalova I, Hola J, Sandula J. **Haemopoiesis-enhancing effects of repeatedly administered carboxymethylglucan in mice exposed to fractionated irradiation.** Folia Biol (Praha). 1995;41(5):249-56. PMID: 8714774 [PubMed - indexed for MEDLINE]	Carboxymethylglucan (CMG), a water-soluble glucan derivative, enhanced the number of granulocytes in the peripheral blood as well as other indices of haemopoietic recovery (total cellularity and the number of granulocyte-macrophage progenitor cells in femoral marrow, spleen weight) investigated after fractionated gamma-irradiation in mice (five doses of 2 Gy each, or three, four and five doses of 3 Gy each given at 24-h intervals). An increased liver weight and a more pronounced anaemia found in the CMG-treated mice suggested, however, that also inflammatory side effects were evoked by the repeated administration of CMG. On the other hand, the development of tolerance, i.e., a decreased effectiveness of the treatment with CMG upon its repeated administration, did not seem to play any major role under the experimental conditions studied, because the protective effects of CMG increased with the increasing number of CMG injections.
Hofer M, Pospisil M, Viklicka S, Pipalova I, Hola J, Netikova J, Sandula J. **Effects of postirradiation carboxymethylglucan administration in mice.** Int J Immunopharmacol. 1995 Mar;17(3):167-74. PMID: 7558510 [PubMed - indexed for MEDLINE]	The hemopoiesis-enhancing ability of a soluble glucan derivative, i.e. carboxymethylglucan (CMG), was investigated in gamma-irradiated mice. Attention was focused on the usefulness of its single or repeated postirradiation administration. CMG was administered i.p. at (a) single dose of 6 mg 2 h postirradiation, (b) four 6 mg doses in the first 4 days postirradiation, (c) four 1.5 mg doses at the same time intervals. Indices of granulopoiesis and inflammatory side effects (liver weight increase and hepatic granulomas) were investigated in mice irradiated with a sublethal dose of 7 Gy. All three CMG-treated groups of mice were found to exhibit enhanced hemopoietic recovery in comparison with the controls. Although the mice repeatedly given the 6 mg CMG doses showed the most rapid recoveries of all the evaluated parameters of granulopoiesis, the most pronounced hepatic side effects were found in these mice, too. When survival of mice was recorded in lethally (9 Gy) irradiated animals, the best protective response were obtained following the repeated administration of the 1.5 mg CMG dose, the survival by day 30 in this group being significantly higher not only in comparison with the controls but also with the mice repeatedly given the 6 mg dose of CMG. The results suggest that the postirradiation CMG administration can be useful for enhancing radiation suppressed hemopoiesis. However, repeated larger CMG doses may produce side effects which compromise the overall survival of irradiated mice.

Beta 1,3-Glucan Radiation Research

Nakano T, Oka K, Sugita T, Tsunemoto H. **Antitumor activity of Langerhans cells in radiation therapy for cervical cancer and its modulation with SPG administration.** In Vivo. 1993 May-Jun;7(3):257-63. PMID: 8357967 [PubMed - indexed for MEDLINE]	Correlations between infiltration of Langerhans cells (ILC) in tumor tissues and radiation curability were investigated in 449 patients with cervical cancer treated with radiation alone, including 390 squamous cell carcinomas and 59 adenocarcinomas. No significant difference in prognosis was noted in stage I, II, and IV squamous cell carcinomas between positive and negative ILC. However, in the patients with stage III squamous cell carcinoma, a significantly better survival was observed for patients with ILC than for those without, 10 year survival rates being 78% vs. 54%, $P < 0.01$. In adenocarcinoma, the patients with ILC also showed significantly better survival than those without ILC, the 10 years survival rates being 45% vs. 25%, $P < 0.025$. An analysis of failure patterns following radiation treatment demonstrated that the favorable prognosis in patients with ILC in squamous cell carcinoma was due to improvement of local control rates and somewhat lower metastatic rates, whereas in adenocarcinoma it was only due to better local control rate. The ILC was significantly associated with T-cell infiltration in tumor tissues. The immunological stimulation with Sizofiran in 20 patients led to an augmentation of ILC in tumor tissues. The present study suggests that the ILC in cancer tissues improves local response to radiation treatment partly by T-cell mediated anti-tumor activity.

Beta 1,3-Glucan Radiation Research

Glucan Source: Schizophyllan (SPG)	
Citation	**Abstract**
Noda K, Takeuchi S, Yajima A, Akiya K, Kasamatsu T, Tomoda Y, Ozawa M, Sekiba K, Sugimori H, Hashimoto S, et al. **Clinical effect of sizofiran combined with irradiation in cervical cancer patients: a randomized controlled study. Cooperative Study Group on SPG for Gynecological Cancer.** Jpn J Clin Oncol. 1992 Feb;22(1):17-25. PMID: 1573785 [PubMed - indexed for MEDLINE]	To evaluate the clinical effect of a biological response modifier (BRM), sizofiran (SPG), combined with irradiation, a randomized controlled study was performed in patients with stage II or III cervical cancer involving the collaboration of 52 institutes throughout Japan. Patients were randomly allocated to the control group (radiotherapy only) and the SPG group (radiotherapy + SPG). SPG was given intramuscularly, 40 mg once and 20 mg twice, a week concomitantly with radiotherapy. A total 315 patients were enrolled for the study but 23 were excluded from analysis. Of the remaining 292 patients, 121 were of stage II (43 controls and 78 SPG) and 171 of stage III (49 controls and 122 SPG). The results were as follows. (1) The complete response (CR) rate among stage II patients was higher in the SPG group (91.0%) than in the control group (79.1%); also the CR rate among stage III patients was significantly higher in the SPG group (77.9%) than in the control group (61.2%). (2) The SPG group showed a significantly rapid recovery from the decreased lymphocyte counts due to radiotherapy (P less than 0.05). (3) Side effects, probably associated with SPG administration, were observed in 11 cases (5.2%). Publication Types: Clinical Trial, Randomized Controlled Trial
Arika T, Amemiya K, Nomoto K. **Combination therapy of radiation and Sizofiran (SPG) on the tumor growth and metastasis on squamous-cell carcinoma NR-S1 in syngeneic C3H/He mice.** Biotherapy. 1992;4(2):165-70. PMID: 1622736 [PubMed - indexed for MEDLINE]	The efficacy of Sizofiran(SPG), a highly purified beta-1,3-D-glucan from the culture broth of basidiomycetes Schizophyllum commune Fries, in combination with local irradiation was investigated using squamous-cell carcinoma NR-S1 and syngeneic hosts of C3H/He mice. NR-S1 tumor was implanted sc in the thigh of C3H/He mice. When tumor grew to 4 mm in diameter, the local irradiation of 55 Gy was delivered. SPG was injected im at a dose of 5 mg/kg. When SPG was administered after irradiation, remarkable inhibition of tumor growth was observed in comparison with the radiation alone group. Furthermore, the combination effect of radiation and active immunotherapy using mitomycin C-treated NR-S1 cells as vaccine was examined. When radiotherapy and active immunotherapy were combined with SPG, suppression of tumor growth was observed from an early stage in comparison with the group which was not administered SPG. SPG also inhibited the pulmonary metastasis of NR-S1 tumor after radiotherapy.
Sekiguchi I, Suzuki M, Izumi A, Aida I, Tamada T. **The study on the immunological effect of sizofilan combined with radiotherapy in patients with uterine cervical cancer.** Nippon Gan Chiryo Gakkai Shi. 1990 Nov 20;25(11):2659-64. Japanese. PMID: 2126027 [PubMed - indexed for MEDLINE]	To investigate the immunological effect of Sizofilan (SPG) combined with radiotherapy, we evaluated the immunological parameters in 22 patients with uterine cervical cancers. Twelve cases were treated with SPG combined with radiotherapy (SPG group), and the other ten cases, with radiotherapy only (control group). As a result, 1) During radiotherapy, the numbers of lymphocyte and CD2 positive cell decreased in SPG and control groups. After radiotherapy, however, its numbers in SPG group became significantly higher than in control group (p less than 0.05). The number of CD3 positive cell also presented a tendency to increase after radiotherapy in SPG group. As for CD20 positive cell, its numbers were kept unchanged after radiotherapy in both two groups, and no significant difference was observed between them. 2) NK cell activity decreased during radiotherapy in both two groups. After radiotherapy, its activity in SPG group recovered to its pre-value and became significantly higher than that in control group (p less than 0.05). 3) SPG did not any prominent effect on CD4/CD8 ratio. 4) The adverse effect of SPG to liver or kidney function were not observed in our patients. The SCC level in SPG group decreased rapidly by radiotherapy as well as that in control group, and no significant difference was observed in SCC levels between them. So it was suggested that SPG did not suppress the cytocidal effect of radiation to cancer cells. Based on these findings, it was concluded that SPG prompted the recovery of not only lymphocyte, especially T cell, but also NK cell activity. These immunological findings presented a usefulness of clinical application of SPG to radiotherapy in patients with uterine cervical cancers.

Beta 1,3-Glucan Radiation Research

Inomata T, Ogawa Y, Nishioka A, Maeda T, Seguchi H. **Improvement in the effects of radiation therapy with BRM.** Gan No Rinsho. 1990 Oct;36(13):2278-85. Japanese. PMID: 2123503 [PubMed - indexed for MEDLINE]	The effects of radiation therapy and Sonifilan (SPG; a glucan produced by Schizophyllum commune) on the control of the primary lesion of human uterine cervix cancer and the experimental metastasis with mice were studied. SPG had excellent effects on the uterine cervix cancer compared with radiation therapy alone. Furthermore, immunohistochemical study showed that tumor infiltrated monocytes in good responders were mainly occupied with helper/induced T lymphocytes. SPG also suppressed the experimental lung metastasis especially with radiation therapy. Metastatic tumor infiltrated monocytes were many macrophages, which was the same as in inoculated local tumor.
Inomata T, Goodman GB, Fryer CJ, Chaplin DJ, Palcic B, Lam GK, Nishioka A, Ogawa Y. **Immune reaction induced by X-rays and pions and its stimulation by schizophyllan (SPG).** Br J Cancer Suppl. 1996 Jul;27:S122-5. PMID: 8763863 [PubMed - indexed for MEDLINE]	Female C57BL/6 mice aged 6-8 weeks with transplanted Lewis lung cancer cells were used to investigate the anti-tumour effects and immune reactions in tumour tissue induced by X-ray and pion irradiation and their modification by schizophyllan (SPG). The effect of SPG on the rate of lung metastasis and the survival time of the mice was also studied using the same tumour system. These studies showed that in this tumour system the "practical' relative biological effectiveness (RBE) of pions was 1.33 in the dose ranges used (3 Gy x 4 = P3; 6 Gy x 4 = P6). SPG increased the suppression of tumour growth associated with moderate doses of radiation: X-rays (4 Gy x 4 = X4) or P3. SPG also decreased the number of lung metastases and prolonged the life span of the mice, these effects being independent of radiation. The addition of SPG to radiation increased both the macrophage infiltration and T-lymphocyte infiltration in the local tumour and the lung nodules. There did not appear to be any major differential effect of SPG on the pion-treated mice compared with those treated with X-rays.

Citation	Abstract
Maisin JR, Albert C, Henry A. **Reduction of short-term radiation lethality by biological response modifiers given alone or in association with other chemical protectors.** Radiat Res. 1993 Sep;135(3):332-7. PMID: 8397428 [PubMed - indexed for MEDLINE]	The advantages gained by a combined treatment of different chemical protectors on short-term lethality of X-irradiated adult male mice have been studied. The following compounds were given alone or in a mixture of two or three compounds: 16,16-dimethyl PGE2 (PGE2), cysteine (Cys), glucan, glutathione (GSH), 5-hydroxytryptamine (5-HT), mercaptoproprionylglycine (MPG), or WR-2721. The survival of mice treated before X irradiation with the optimal dose of each radioprotector given separately shows that WR-2721 and 5-HT yield the best protection with dose reduction factors (DRFs) of 2.2 and 1.7, respectively. Cysteine, glucan, PGE2, MPG, and GSH, with DRFs of 1.4, 1.4, 1.2, 1.1, and 1.1, respectively, are less efficient radioprotectors. When PGE2 was combined with a low dose of WR-2721 (200 mg/kg), the protection increased in a synergistic way. The increase in protection offered by a combination of PGE2 with Cys, glucan, GSH, or 5-HT is less marked and the effect obtained is only additive. A synergistic action is also obtained with a combination of WR-2721 (200 mg/kg) and 5-HT (8 mg/kg) (DRF 2.7).
Hofer M, Pospisil M, Viklicka S, Vacek A, Pipalova I, Bartonickova A. **Hematopoietic recovery in repeatedly irradiated mice can be enhanced by a repeatedly administered combination of diclofenac and glucan.** J Leukoc Biol. 1993 Feb;53(2):185-9. PMID: 8445330 [PubMed - indexed for MEDLINE]	A combination of diclofenac and glucan administered repeatedly in a protective regimen in the course of repeated gamma irradiation of mice (6 x 2 Gy during 3 weeks) enhanced granulopoiesis and other indices of hematopoietic recovery investigated from 3 to 7 days after the last radiation exposure. Repeated administration of diclofenac or glucan alone or treatment of the mice with the diclofenac-glucan combination given once before the first or the last radiation exposure did not induce such effects. The protective effect of the repeatedly administered combination of the drugs was realized despite the fact that the response of the serum colony-stimulating activity to the repeated combined drug administration was decreased at the end of the treatment regimen compared to that of mice given this drug combination only once. The combined treatment is supposed to act via increased proliferation of the hematopoietic stem or progenitor cells. Additivity or even synergism of the hematostimulatory action of glucan and of the strengthening of positive control of cell proliferation achieved by removing negatively acting prostaglandins (diclofenac action) may account for the radioprotective effects observed.

Beta 1,3-Glucan Radiation Research

Walinder G, Arora RG, Bierke P, Broome-Karlsson A, Svedenstal BM. **Effects of glucan on the reticuloendothelial system and on the development of tumors in 90Sr-exposed mice.** Acta Oncol. 1992;31(4):461-7. PMID: 1632983 [PubMed - indexed for MEDLINE]	A series of experiments was conducted to examine the effect of glucan on the reticuloendothelial system (RES) and on the development of 90Sr-induced osteosarcomas and malignant lymphomas in CBA/S mice. Glucan demonstrated a strong RES-stimulating effect, as evidenced by a dose-related increase in lysozyme levels in the plasma and an enlargement of the liver and spleen. Weekly injections of glucan between 150 and 250 days after exposure to 90Sr suppressed the actuarial appearance of the fibroblastic type of osteosarcomas and stimulated the emergence of malignant lymphomas. Glucan itself had no tumorigenic effect in mice not exposed to 90Sr.
Chorvatovicova D. **Suppressing effects of glucan on micronuclei induced by Co60 in mice.** Strahlenther Onkol. 1991 Oct;167(10):612-4. PMID: 1948647 [PubMed - indexed for MEDLINE]	The effects of glucan on the frequency of micronuclei in polychromatic erythrocytes of A/Ph mouse bone marrow induced by Co60 irradiation were examined. Suppressing effect of three glucan derivatives was statistically significant (P less than 0.01) by intravenous application of glucan one hour after irradiation. The most expressive effect was obvious by K3 substituent (DS 0.89). Intraperitoneal application of glucan has to be done earlier than one hour after irradiation. The suppressive effects of glucans can be explained by their ability to trap OH radicals and so decrease the clastogenic effect of irradiation. The results may be useful for therapeutic application of glucan with radiation therapy.