

Special Report



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Welcome

Learn how the Immune System works and how to improve it in 30 days utilizing Glucanol™ Immune Support Supplement. This process is a clinically proven solution for a healthy and strong immune system.



Glucanol™
Information Center



HOW THE IMMUNE SYSTEM WORKS AND HOW TO IMPROVE IT IN 30 DAYS

GLUCANOL™ IMMUNE SUPPORT SUPPLEMENT

A CLINICALLY PROVEN SOLUTION FOR A HEALTHY AND STRONG IMMUNE SYSTEM

Inside:

Find Out How Glucanol™ Works and Read About All Of The Research Done And Reported In Peer Reviewed Journal Articles. Read This Bibliography. Your Future Health Will Depend Upon It.

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The Glucanol™ Story

The revolutionary, pharmaceutical grade ingredients in Glucanol™ engages the body's natural defenses to protect it against a wide range of challenges. Our ingredients have a clinically proven mechanism of action that activates innate immune cells to move faster to the site of a challenge and more quickly recognize and destroy foreign intruders.

Efficacy

- *Glucanol™ Increases Microbial Killing.* In clinical studies, Glucanol's™ highly purified and biologically active 1-3,1-6 beta glucan significantly increased phagocytic capacity, the ability of the innate immune cells to eat and destroy foreign intruders. After 10 days of treatment, Glucanol™ had increased the percentage of immune cells able to phagocytose one particle from 63.8% to 83.2% (P< .05). The number of highly phagocytic cells increased from 37.3% to more than 50% (P< .05).
- *Glucanol™ Increases Immune Cell Activity.* A placebo-controlled, double-blinded clinical study conducted with 62 subjects to assess the impact of the ingredients in Glucanol™ on immune biomarkers for subjects exposed to rhinovirus (common cold) was conducted. Generally, the immune system responds to viral infections with an increase in Natural Killer (NK) cells and cytotoxic T cells as primary defense mechanisms. Participants receiving Glucanol's™ ingredient had more NK cells and cytotoxic T Cells (12.5%) as a percent of all lymphocytes than participants in the control group (9.8%).
- *Glucanol™ Enhances Immune Cell Migration to Site of Challenge.* Glucanol's™ active form enhances the ability of certain human immune cells to migrate to the site of a bacterial infection. Neutrophils, the most abundant type of innate immune cell in the body, are attracted to the site of an infection by blood proteins called chemo-attractants and are among the first cells of the body to respond to a challenge due to infection or injury. Priming neutrophils with Glucanol's™ pharmaceutical grade 1-3,1-6 beta glucan increases their ability to sense complement fragments emanating from the site of an infection. As a result, a more rapid immune response to infection results in faster microbial clearance and healing.

Safety

Studies demonstrate Glucanol™ safely enhances and supports healthy immune system function.

- Animal tox studies with doses ranging from 0 to 1,000 times recommended daily dose.
- Human studies with doses up to 60 times recommended daily dose.
- No increase in tested cytokines or other adverse effects.
- Glucanol™ increased ability of human immune cells to kill foreign challenges.

Overview

Manipulating the immune system for human health benefits is not new. Vaccines have been used for decades for preventative purposes. Research and development efforts are increasingly being focused on immunotherapy

drugs to treat disease by directly activating the immune response to a specific target. In the last 20 years, there has been significant development in immunotherapy for the treatment of cancer.

The immune system consists of two major subsystems: innate immunity and acquired (adaptive) immunity. As its name implies, innate immunity is the protection we are born with. Innate immune cells are the body's first line defenders. Innate immune cells attack pathogens in a non-discriminatory manner. Adaptive immunity is learned. The adaptive immune system recognizes molecules unique to a foreign pathogen and maintains a "memory" of these pathogens so it can respond more quickly to a subsequent infection.

Most pharmaceutical development, however, has been focused on utilizing the adaptive arm of the immune system (e.g. vaccines, antibodies, T-cells, B-cells). Recently, pharmaceutical companies have placed greater focus on compounds that can activate the innate immune system (e.g. toll-like receptors, growth factors, cytokines) to work in combination with the adaptive immune system for a more complete immune response against disease.

Glucanols™ technology is focused on the innate immune system. The significance of the technology is its ability to enhance the natural innate immune function and in certain circumstances, engage and direct the innate immune cells in novel ways against specific diseases. In these targeted applications, Glucanol™ acts as a keystone, engaging both the innate and adaptive immune systems to work in concert for a more complete immune response.

The Immune System

The human immune system is a network of cells and proteins that interact to protect against foreign challenges. This complex system is subdivided into innate and adaptive immune systems. The innate immune system is the first line of defense against pathogens and is characterized as "non-specific" because it functions against pathogens in general. Adaptive immunity is initiated following the activation of the innate system and is characterized as "specific," because it generates long lasting immunological memory to specific antigens within the foreign pathogens or on their surface. There are hundreds of different types of receptors on the surface of immune cells that control and activate the complex cellular and molecular interactions between these two subsystems. In real-life, these two arms work in concert to protect the body from health challenges.

The innate immune system is composed of billions of white blood cells that are the body's first line of defense. These cells, which can distinguish between self and non-self, patrol the body in search of foreign pathogens such as bacteria, viruses and cancer cells. Once such invaders are detected, cells of the innate immune system respond rapidly (in minutes or hours) with a number of non-specific killing mechanisms designed to destroy the intruding organisms or cells. Innate immune cells also play an important role in initiating the adaptive immune response which is slower (in days or weeks) yet generates a specific killing mechanism targeting a particular intruding organism, such as a specific bacteria or virus or cancer cell.

Glucanol™ and PAMPs

Although the innate immune system is considered "non-specific," it does recognize highly conserved, pathogen-specific molecules known as Pathogen Associated Molecular Patterns (PAMPs). Innate immune response is often initiated by the binding of PAMPs to select receptors on innate immune cells. Simply put, PAMPs are natural molecular structures that the innate immune system uses to recognize foreign pathogens and to trigger innate immune cells to kill the pathogen and to activate the adaptive immune system.

This process of recognition is mediated through several receptors found on innate immune cells. Functionally, the immune response can differ depending on what type of immune cell and which receptor the PAMP is bound to and whether it is bound by an individual receptor or multiple receptors at the same time. Receptor binding of PAMPs can trigger an immune response that includes engulfing or eating the pathogen (phagocytosis), sending chemical messages called “cytokines” to other immune cells to activate them, and killing the pathogen or cancer cell. GlucanTM activates this innate immune cell function against other disease targets.

The technology used in GlucanTM involves natural PAMP structures found in the cell walls of yeast. These compounds are chains of glucose molecules (polysaccharides or glucans) connected by a very specific linkage pattern (beta 1,3/1,6 glucan). There has been significant research published on the ability of PAMPs to induce immune responses. GlucanTM utilizes patented technology surrounding the production, purification, and characterization of natural PAMP molecules that can be used as immune modulators. The binding of these molecules to specific receptors on innate immune cells activates select immune responses that can be used to target various diseases.

This technology includes a number of patented polysaccharide compounds that are well characterized as to form, size and shape. The research supported by patents held by Biothera Pharma has identified the specific mechanism of action of these compounds. The significance of the technology is that these compounds each have unique molecular features that result in their ability to bind to specialized innate immune cell receptors that can trigger select immune responses. Research has demonstrated that when these compounds are used in combination with certain drug therapies, they have a synergistic effect leading to significantly enhanced efficacy. The result is a platform technology with the potential to be used in multiple combination therapies against multiple disease indications.

Bibliography

The bibliography below is separated by disease state or 1-3, 1-6 beta glucan effect. You will see the same citation under a number of headings because the research produced results that were important for each. This peer reviewed research touches important topics such as:

Adjuvants	Fungal Disease and Pathogens
Aging	Hemopoietic Recovery
Antibiotics	Hepatitis – Viral
Antimicrobial Activity	Immune Response Potentiation
Antioxidants	Impaired Immunity
Anthrax	Infections
Arthritis	Irradiation Injury
Atherosclerosis	Leukemia
Bacterial Infection	Lipid Metabolism
Bone Marrow Injury	Liver Damage
Burn – Oxidative Organ Damage	Macrophage Activation
Cancer	Melanoma
Cancer – Carcinoma of the Breast	Methotrexate Toxicity
Cancer – Ovarian	Mycotoxins
Cancer – Sarcoma	Oxidative Damage
Cancer – Sarcoma and Melanoma	Parasites
Cancer – Radiotherapy	Platelet Recovery
Candida albicans	Pneumonia
Chemotherapy	Radiation Damage Protection

Cholesterol Control	Rheumatoid Arthritis
Chronic Fatigue Syndrome	Safety – FDA Classification
Coronary Artery Disease	Spinal Cord Injury
Diabetes/Glucose Control	Stem Cell Transplantation
Escherichia coli	Trauma
Free Radical Scavenger	Tumors
	Viral Infections
	White Blood Cell Recovery
	Wound Healing

Acetaminophen Liver Toxicity:

Toklu HZ, Sehirili AO, Velioglu-Ogunc A, Centinel S, Sener G; "Acetaminophen-induced toxicity is prevented by beta-d-glucan treatment in mice." *European J Pharmacology*; 543(1-3):133-40; Epub 2006 Jun; Jun 2, 2006. **Direct Quote:** *"The protective effect of beta-glucan against oxidative injury caused by acetaminophen [Tylenol, Anacin 3, Tempra, Datril] was studied in mice liver...Acetaminophen caused a significant decrease in the GSH level of the tissue, which was accompanied with significant increases in the hepatic luminol and lucigenin chemiluminescence values, malondialdehyde level, MPO activity and collagen content. Similarly, serum ALT, AST levels, as well as LDH and TNF-alpha, were elevated in the acetaminophen-treated group...beta-d-glucan treatment reversed all of these [liver toxicity] biochemical indices, as well as histopathological alterations that were induced by acetaminophen. In conclusion, these results suggest that beta-d-glucan exerts cytoprotective effects against oxidative injury through its antioxidant properties and may be of therapeutic use in preventing acetaminophen toxicity."*

Adjuvants

Guzel S, Sunamak O, AS A, Celik V, Ferahman M, Nuri MM, Gazioglu E, Atukeren P, Mutlu O; "Effects of hyperbaric oxygen and Pgg-glucan on ischemic colon anastomosis." *World J Gastroenterol*; 7:12(9):1421-5. Mar 2006. **Direct Quote:** *"... Here we analyzed the effects of hyperbaric oxygen and beta-glucan on colon anastomoses in ischemic condition. ... CONCLUSION: Hyperbaric oxygen and glucan improve healing in ischemic colon anastomoses [surgical connection of two parts of the colon together] by anti-microbic, immune stimulating properties and seem to act synergistically when combined together."*

Tzianabos AO, Cisneros RL; "Prophylaxis with the immunomodulator PGG glucan enhances antibiotic efficacy in rats infected with antibiotic-resistant bacteria," *Ann NY Acad Sci* 797: 285-287; Oct 1996. **Direct Quote:** *"Results of these studies demonstrated that prophylaxis with PGG glucan in combination with antibiotics provided enhanced protection against lethal challenge with Escherichia coli or Staphylococcus aureus as compared with the use of antibiotics alone."*

Jamas S, Easson D, Ostroff G: "Underivatized aqueous soluble beta (1,3) glucan, composition and method of making same." U.S. Patent Application 20020032170, March 14, 2002. **Direct Quote:** *"The*

use of soluble and insoluble beta glucans alone or as vaccine adjuvants for viral and bacterial antigens has been shown in animal models to markedly increase resistance to a variety of bacterial, fungal, protozoan and viral infections."

Wyde, P., "Beta-1,3-glucan activity in mice: intraperitoneal and oral applications." Baylor College of Medicine Research Report. 1989. **Direct Quote:** *"This demonstration of bactericidal enhancement via oral dosing suggests an application for beta-1,3-glucan as a component in a combined modality with conventional anti-infective agents. Beta glucan, through the stimulation of host defense systems, creates a more supportive environment within the body to assist the primary killing action of the conventional agent."*

Sener G, Sert G, Ozer SA, Arbak S, Uslu B, Gedik N, Avanoglu-Dulger G; "Pressure ulcer-induced oxidative organ injury is ameliorated by beta-glucan treatment in rats." Int Immunopharmacol:6(5):724-32; Marmara U, Sch of Pharmacy, Dept Pharmacology, Div Biochemistry; Epub Nov 2005; May 2006. **Direct Quote:** *"Pressure ulcers (PU) cause morphological and functional alterations in the skin and visceral organs. ... Local treatment with beta-glucan inhibited the increase in MDA and MPO levels and the decrease in GSH in the skin induced by (PU), systemic treatment prevented the damage in the visceral organs. Significant increases in creatinine, BUN, ALT, AST, LDH and collagen levels in PU [Pressure Ulcers] group were prevented by beta-glucan treatment. ... Tissue injury was decreased. ... Thus, supplementing geriatric and neurologically impaired patients with adjuvant therapy of beta-glucan may have some benefits for successful therapy and improving quality of life."*

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Aging :

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Carrow, D.J. M.D.; "Beta-1,3-glucan as a Primary Immune Activator," Townsend Letter; June 1996. **Direct Quote:** *"The following list includes benefits from the use of Beta 1,3-glucan supplementation: People who have impaired immunity from any cause ...; have a high occurrence of infectious diseases; have tumors and/or those undergoing chemotherapy or radiation therapy; are over forty who are concerned about the natural aging process or might have noticed a slowing down of immune reactivity; who are geriatric patients; and other with compromised immune disorders."*

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European J Pharmacology; 542(1-3):170-178; Epub May 2006. Aug 7 2006. **Direct Quote:**

"Methotrexate is an antifolate [antimetabolite chemotherapy drug] that is widely used in the treatment of rheumatic disorders and malignant tumors. The efficacy of methotrexate is often limited by severe side effects and toxic sequelae [disease condition caused by a disease], where oxidative stress [free radical damage] is noticeable. ... Thus, the findings of the present study suggest that beta-glucan, through its antioxidant and immunoregulatory effects, may be of therapeutic value in alleviating the leukocyte apoptosis [white immune cell death], oxidative [free radical] tissue injury and thereby the intestinal and hepatorenal [liver or kidney] side effects of methotrexate treatment."

Toklu HZ, Sehirili AO, Velioglu-Ogunc A, Centinel S, Sener G; "Acetaminophen-induced toxicity is prevented by beta-d-glucan treatment in mice." European J Pharmacology; 543(1-3):133-40; Epub 2006 Jun; Jun 2, 2006. **Direct Quote:** **"The protective effect of beta-glucan against oxidative injury caused by acetaminophen [Tylenol, Anacin 3, Tempra, Datri] was studied in mice liver...Acetaminophen caused a significant decrease in the GSH level of the tissue, which was accompanied with significant increases in the hepatic luminol and lucigenin chemiluminescence values, malondialdehyde level, MPO activity and collagen content. Similarly, serum ALT, AST levels, as well as LDH and TNF-alpha, were elevated in the acetaminophen-treated group...beta-d-glucan treatment reversed all of these [liver toxicity] biochemical indices, as well as histopathological alterations that were induced by acetaminophen. In conclusion, these results suggest that beta-d-glucan exerts cytoprotective effects against oxidative injury through its antioxidant properties and may be of therapeutic use in preventing acetaminophen toxicity."**

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Anthrax:

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infection in mice. The mechanism of action involves the stimulation of three important cytokines: IL-2, IFN- γ , and TNF- α ."

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Wyde, P., "Beta-1,3-glucan activity in mice: intraperitoneal and oral applications." Baylor College of Medicine Research Report. 1989. **Direct Quote: "This demonstration of bactericidal enhancement via oral dosing suggests an application for beta-1,3-glucan as a component in a combined modality with conventional anti-infective agents. Beta glucan, through the stimulation of host defense systems, creates a more supportive environment within the body to assist the primary killing action of the conventional agent"**.

Beta Glucan Toxicity:

Li B, Allendorf D, Hansen R, Marroquin J, Ding C, Cramer DE, Yan J; "Yeast beta-Glucan Amplifies Phagocyte Killing of iC3b-Opsonized Tumor Cells via Complement Receptor 3-Syk-Phosphatidylinositol 3-Kinase Pathway." *J Immunology*: 1:177(3):1661-9. Tumor Immunobiology Program, James Graham Brown Cancer Center, University of Louisville, Louisville, KY. Aug 2006. **Direct Quote: "Anti-tumor mAbs [monoclonal antibodies] hold promise for cancer therapy, but are relatively inefficient. ...In this study, we report that tumor-bearing mice treated with a combination of beta-glucan and an anti-tumor mAb show almost complete cessation of tumor growth. beta-glucan, an agent without evident toxicity, may be used to amplify tumor cell killing and may open new opportunities in the immunotherapy of cancer."**

Bone Marrow Injury:

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Cancer:

Li B, Allendorf D, Hansen R, Marroquin J, Ding C, Cramer DE, Yan J; "Yeast beta-Glucan Amplifies Phagocyte Killing of iC3b-Opsonized Tumor Cells via Complement Receptor 3-Syk-Phosphatidylinositol 3-Kinase Pathway." J Immunology: 1:177(3):1661-9. Tumor Immunobiology Program, James Graham Brown Cancer Center, University of Louisville, Louisville, KY. Aug 2006. **Direct Quote:** "*Anti-tumor mAbs [monoclonal antibodies] hold promise for cancer therapy, but are relatively inefficient. ...In this study, we report that tumor-bearing mice treated with a combination of beta-glucan and an anti-tumor mAb show almost complete cessation of tumor growth. beta-glucan, an agent without evident toxicity, may be used to amplify tumor cell killing and may open new opportunities in the immunotherapy of cancer.*"

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Murine Tumor Models," The J of Immunology 173:797-806. James Graham Brown Cancer Ctr, Louisville, KY; July 15, 2004: **Direct Quote:** "*Orally administered B-1,3-glucans were taken up by macrophages that transported them to spleen, lymph nodes, and bone marrow. Within the bone marrow, the macrophages degraded the large B-1,3 glucans into smaller soluble B-1,3-glucan fragments that were taken up by the CR3 [receptors] of marginated granulocytes [white blood cells formed in the bone marrow]. These granulocytes with CR3-bound B-1,3-glucan-fluorescein were shown to kill iC3b-opsonized tumor [cancer] cells following their recruitment to a site of complement activation resembling a tumor coated with mAB [monoclonal antibodies].*"

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in the tumor cell loss from the lungs of ...mice challenged respectively with intravenous 125IuDR labelled B16 or T 1699 mammary carcinoma cells."

Cancer – Ovarian:

Kobayashi H, Yoshida R, Kanada Y, Fukuda Y, Yagyu T, Inagaki K, Kondo T, Kurita N, Suzuki M, Kanayama N, Terao T., "Suppressing effects of daily oral supplementation of beta-glucan extracted from *Agaricus blazei* Murill on spontaneous and peritoneal disseminated metastasis in mouse model." Dept of Obstetrics and Gynecology, Hamamatsu U Sch of Med; J Cancer Res Clin Oncol. 5 May 10, 2005. **Direct Quote:** "**Results: ... (1) beta-glucan had cytotoxic effect against human ovarian cancer HRA cells in vitro; (2) beta-glucan promotes p38 MAPK activity for suppressing HRA cell proliferation and amplifying the apoptosis cascade. Conclusion: Treatment with beta-glucan may be beneficial for cancer patients with or at risk for metastasis.**"

Cancer-Sarcoma:

Sveinbjornsson B, Olsen R, et al, "Macrophage cytotoxicity against murine meth A sarcoma involves nitric oxide-mediated apoptosis." Biochem Biophys Res Commun. Jun 25;223(3):643-9; Jun 1996. **Direct Quote:** "**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.**"

Cancer – Sarcoma and Melanoma:

Williams DL, et al, "Therapeutic efficacy of glucan in a murine model of hepatic metastatic disease," Hepatology 5(2):198-206. Mar 1985. **Direct Quote:** "**...coincubation of particulate glucan with diverse populations of normal or tumor cells in vitro indicated that glucan exerted a direct cytostatic effect on sarcoma and melanoma cells and, in contrast, had a proliferative effect on normal spleen and bone marrow cells.**"

Cancer – Sarcoma:

Seljelid R, et al, "Evidence that tumor necrosis induced by an irradiated beta 1-3D polyglucose is mediated by a concerted action of local and systemic cytokines," Scand J Immuno 30(6): 687-694. Dec 1989 **Direct Quote:** "**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 [in the body] and in macrophage cultures in vitro [out of body].**"

Cancer - Radiotherapy:

Gu YH, Takagi Y, et al; "Enhancement of radioprotection and anti-tumor immunity by yeast-derived beta-glucan in mice," J Med Food. 8(2) 154-8; Dept of Radiological Technology, Suzuka U of Med Sc,

Suzuka, Japan, Summer 2005. **Direct Quote:** *"Intraperitoneal injection of beta-glucan was shown to greatly delay mortality in mice exposed to whole-body X-ray radiation and tumor growth in tumor-bearing mice. ...Augmented immunological activity as seen in increased NK (natural killer) and LAK (lymphokine-activated killer) activity by beta-glucan seems to play a role in preventing secondary infections associated with irradiation and probably contributes to the attenuated [reduced] tumor growth in tumor-bearing mice through enhanced anti-tumour immunity. These results suggest that beta-glucan may be a promising adjunct treatment for cancer patients receiving radiotherapy."*

Cancer : Radiation Damage

Carrow, D.J.; "Beta-1,3-glucan as a Primary Immune Activator," Townsend Letter; June 1996. **Direct Quote:** *"Over the past 11 months I have been able to convince five out of eight breast cancer patients who were undergoing radiation therapy, to consume one capsule of beta 1,3/1,6 glucan (NSC-24 3 mg) three times per day. To date, I have observed that none of the patients using NSC-24 have suffered from any type of radiation injury to the skin, while the three patients who chose not to use NSC-24 all show signs of extensive radiation damage to the skin."*

Kobayashi H, Yoshida R, Kanada Y, Fukuda Y, Yagyu T, Inagaki K, Kondo T, Kurita N, Suzuki M, Kanayama N, Terao T., "Suppressing effects of daily oral supplementation of beta-glucan extracted from *Agaricus blazei* Murill on spontaneous and peritoneal disseminated metastasis in mouse model." Dept of Obstetrics and Gynecology, Hamamatsu U Sch of Med; J Cancer Res Clin Oncol. 5 May 10, 2005. **Direct Quote:** *"Conclusion: Treatment with beta-glucan may be beneficial for cancer patients with or at risk for metastasis."*

Williams D.L., Browder I. and DiLuzio N.R., "Methods and compositions for prophylactic and therapeutic treatment of infections," U.S. Patent 4900722, Issued Feb 13, 1990. **Direct Quote:** *"The soluble phosphorylated glucans are also useful for stimulating macrophage cells, either in vivo or in vitro, to produce a cytotoxic/cytostatic factor effective against cancer cells."* [cytotoxic: toxic to cell - prevents reproduction or growth]

Sveinbj B, Seternes O, Seljelid R, "Macrophage cytotoxicity against murine meth A sarcoma involves nitric oxide-mediated apoptosis," Biochem Biophys Res Commun, 223:3, 643-9. Jun 1996. **Direct Quote:** *"When stimulated with interferon-gamma and soluble beta 1,3-D-glucan, macrophages exerted cytotoxicity towards syngeneic Meth A [sarcoma] tumor cells."*

Candida albicans, Staphylococcus and Infectious Challenge:

Rice PJ, Adams EL, Ozment-Skelton T, Gonzales A, Goldman MP, Lockhart BE, Barker LA, Breuel KF, Deponti WK, Kalbfleisch JH, Ensley HE, Brown GD, Gordon S, Williams DL.; "Oral delivery and gastrointestinal absorption of soluble glucans stimulate increased resistance to infectious challenge." East Tennessee State University. J Pharmacol Exp Ther. Jun 23, 2005. **Direct Quote:** *"Oral glucan administration also increased survival in mice challenged with Staphylococcus aureus or Candida albicans ...[and] increase[s] IL-12 expression and induce[s] protection against infectious challenge."*

Candida albicans:

Gantner BN, Simmons RM, Underhill DM. "Dectin-1 mediates macrophage recognition of *Candida albicans* yeast but not filaments"; The Department of Immunology, University of Washington, Seattle, WA, Embo J; 23:24(6):1277-86, Mar 2005; **Direct Quote:** "**Dectin-1 is a receptor that binds beta-glucans and is important for macrophage phagocytosis of fungi. ... the normal mechanisms of yeast budding and cell separation create permanent scars which expose sufficient beta-glucan to trigger antimicrobial responses through Dectin-1, including phagocytosis and activation of reactive oxygen production [anti-oxidant - free radical neutralization].**"

Browder IW., et al., "Modification of Post-Operative *C. albicans* Sepsis by Glucan Immunostimulation," Int. J. Immunopharmac.; 6:19-26. Dept of Surg and Physiol, Tulane U Sch of Med, LA; 1984. **Direct Quote:** "**Protection against *C. albicans* was observed in the glucan-treated groups. ... These observations suggest that Biologic Response Modifiers such as glucan may be effectively employed in patients who are at risk for post-operative infections.**"

Chemotherapy:

Sener G, Eksioglu-Demiraop E, Cetiner M, Ercan F, Yegen BC; "beta-glucan ameliorates methotrexate-induced oxidative organ injury via its antioxidant and immunomodulatory effects." European J Pharmacology; 542(1-3):170-178; Epub May 2006. Aug 7 2006. **Direct Quote:** "**Methotrexate is an antifolate [antimetabolite chemotherapy drug] that is widely used in the treatment of rheumatic disorders and malignant tumors. The efficacy of methotrexate is often limited by severe side effects and toxic sequelae [disease condition caused by a disease], where oxidative stress [free radical damage] is noticeable. ... Thus, the findings of the present study suggest that beta-glucan, through its antioxidant and immunoregulatory effects, may be of therapeutic value in alleviating the leukocyte apoptosis [white immune cell death], oxidative [free radical] tissue injury and thereby the intestinal and hepatorenal [liver or kidney] side effects of methotrexate treatment.**"

Tohamy AA et al. "Beta-glucan inhibits the genotoxicity of cyclophosphamide, adriamycin and cisplatin." Mutat. Research. 541(1-2):45-53. Nov 2003. **Direct Quote:** "**This protective effect of beta-glucan could be attributed to its scavenging ability to trap free-radicals produced during the biotransformation of these anti-neoplastic [abnormal tissue growth] drugs. Beta-glucan also markedly restored the mitotic [cell division] activity of bone marrow cells that had been suppressed by the anti-neoplastic drugs. These results indicate that in addition to known immunopotentiating activity of beta-glucan, it plays a role in reducing genotoxicity [capability to cause cancer] induced by anti-neoplastic [abnormal tissue growth] drugs during cancer chemotherapy.**"

Carrow, D.J. M.D.; "Beta-1,3-glucan as a Primary Immune Activator," Townsend Letter; June 1996. **Direct Quote:** "**The following list includes benefits from the use of Beta 1,3-glucan supplementation: People who have impaired immunity from any cause ...; have a high occurrence of infectious diseases; have tumors and/or those undergoing chemotherapy or radiation therapy; are over forty who are concerned about the natural aging process or might have noticed a slowing down of immune reactivity; who are geriatric patients; and other with compromised immune disorders.**"

Cholesterol Control:

Robert Nicolosi, Stacey J Bell, Bruce R Bistran, Isaac Greenberg, R Armour Forse and George L Blackburn, "Cholesterol Benefits from Beta 1,3/1,6 Glucan Purified from Yeast Cell Wall," Nutrition and Infection Laboratory, Harvard Medical School; the Centers for the Study of Nutrition and Medicine and for Nutritional Research, and Clowes Surgical Metabolism Laboratory, Beth Israel Deaconess Medical Center, Boston. American Journal of Clinical Nutrition, Vol. 70, No. 2, 208-212, August 1999.

Direct Quote: *"The purpose of this study was to evaluate the effect on serum lipids of a yeast-derived β -glucan fiber in 15 free-living, obese, hypercholesterolemic men. ... The yeast-derived β -glucan fiber significantly lowered total cholesterol concentrations and was well tolerated... The link between elevated plasma LDL-cholesterol concentrations and the risk of developing coronary artery disease has been clearly established... Elevated plasma cholesterol and, in particular, LDL-cholesterol concentrations are associated with increased risk of coronary artery disease, whereas an elevated of HDL-cholesterol concentration is inversely correlated with the incidence of cardiovascular... The yeast-derived β -glucan fiber lowered total cholesterol and raised HDL-cholesterol concentrations significantly. ... Unlike the significant increases in HDL-cholesterol concentrations observed 4 wk after the end of the study for subjects receiving the yeast-derived β -glucan, none of the 24 studies of oat products reported significant changes in HDL concentration. ... Because higher HDL-cholesterol concentrations are associated with a reduced risk of developing coronary artery disease, there may be unique benefits of using the yeast-derived β -glucan, and perhaps psyllium, rather than the oat products."*

Chronic Fatigue Syndrome:

Uchida, A.; "Method for treatment of chronic fatigue syndrome," U.S. Patent 5424300 (A method for the treatment of chronic fatigue syndrome, comprising administering a polysaccharide which further contains a .beta(1-3)glucan.-1,3/1,6-glucoside bond). Issued June 13, 1995.

Colorectal Surgery:

Guzel S, Sunamak O, AS A, Celik V, Ferahman M, Nuri MM, Gazioglu E, Atukeren P, Mutlu O; "Effects of hyperbaric oxygen and Pgg-glucan on ischemic colon anastomosis." World J Gastroenterol: 7:12(9):1421-5. Mar 2006. **Direct Quote:** *"... Here we analyzed the effects of hyperbaric oxygen and beta-glucan on colon anastomoses in ischemic condition. ... CONCLUSION: Hyperbaric oxygen and glucan improve healing in ischemic colon anastomoses [surgical connection of two parts of the colon together] by anti-microbial, immune stimulating properties and seem to act synergistically when combined together."*

Coronary Artery Disease - Cholesterol Control:

Robert Nicolosi, Stacey J Bell, Bruce R Bistran, Isaac Greenberg, R Armour Forse and George L Blackburn, "Cholesterol Benefits from Beta 1,3/1,6 Glucan Purified from Yeast Cell Wall," Nutrition and Infection Laboratory, Harvard Medical School; the Centers for the Study of Nutrition and Medicine and for Nutritional Research, and Clowes Surgical Metabolism Laboratory, Beth Israel Deaconess Medical Center, Boston. American Journal of Clinical Nutrition, Vol. 70, No. 2, 208-212, August 1999.

Direct Quote: *"The purpose of this study was to evaluate the effect on serum lipids of a yeast-derived β -glucan fiber in 15 free-living, obese, hypercholesterolemic men. ... The yeast-derived β -glucan fiber significantly lowered total cholesterol concentrations and was well tolerated... The link between elevated plasma LDL-cholesterol concentrations and the risk of developing coronary artery disease has been clearly established... Elevated plasma cholesterol and, in particular, LDL-cholesterol concentrations are associated with increased*

risk of coronary artery disease, whereas an elevated of HDL-cholesterol concentration is inversely correlated with the incidence of cardiovascular... The yeast-derived β -glucan fiber lowered total cholesterol and raised HDL-cholesterol concentrations significantly. Unlike the significant increases in HDL-cholesterol concentrations observed 4 wk after the end of the study for subjects receiving the yeast-derived β -glucan, none of the 24 studies of oat products reported significant changes in HDL concentration. ... Because higher HDL-cholesterol concentrations are associated with a reduced risk of developing coronary artery disease, there may be unique benefits of using the yeast-derived β -glucan, and perhaps psyllium, rather than the oat products."

Diabetes / Glucose Control:

Pola P, "Composition for the prevention and/or treatment of lipid metabolism disorders and allergic forms," U.S. Patent Application 20030017999, January 23, 2003. **Direct Quote:** ".beta-1,3-D-glucan has proved effective not only in preventing lipid metabolism disorders, but also in stimulating immune defenses, in preventing onset of tumors and in controlling serum glucose."

Carrow, D.J.; "Beta-1,3-glucan as a Primary Immune Activator," Townsend Letter; June 1996. **Direct Quote:** "The following list includes benefits from the use of Beta 1,3-glucan supplementation: ...people with chronic degenerative disorders such as diabetes or chronic inflammation. ..."

Kida K., Inoue T., et al; "An immunopotentiator of beta-1,6;1,3 D-glucan prevents diabetes and insulinitis in BB rats." Diabetes. Res. Clin. Pract. 17:75-79. 1992. **Direct Quote:** "The preventive effect of an immunopotentiator, beta-1,6;1,3 D-glucan, on the development of diabetes and insulinitis was studied in BB rats...[and] decreased the cumulative incidence of diabetes from 43.3% to 6.7% and also the incidence of insulinitis from 82.4% to 26.3%... These data indicate that immunopotentiators could modulate the autoimmune mechanisms directed to pancreatic islets and inhibit the development of diabetes in BB rats."

Escherichia coli:

Williams D.L, Browder IW and DiLuzio N.R, "Immunotherapeutic modification of Escherichia coli—induced experimental peritonitis and bacteremia by glucan," Surgery 93(3):448-454. Mar 1983.

Direct Quote: "These data denote that the intraperitoneal administration of glucan significantly modifies the course of E. coli-induced peritonitis and bacteremia due, in part, to glucan-induced enhancement of macrophage function."

Onderdonk, A.B., et al., "Anti-Infective Effect of Poly-.beta.1-6 -Glucotrisyl-.beta.1-3-Glucopyranose Glucan In Vivo," Infect. Immun.; 60:1642-1647. 1992. Dept of Pathology, Channing Lab, Brigham and Women's Hospital, Boston, MA. **Direct Quote:** "Mice challenged with Escherichia coli or Staphylococcus aureus were protected against lethal peritonitis by the intravenous administration of 10 micrograms of poly-beta 1-6-glucotriosyl-beta 1-3-glucofuranose (PGG) glucan per animal 4 to 6 h prior to bacterial challenge."

Tzianabos AO, Cisneros RL; "Prophylaxis with the immunomodulator PGG glucan enhances antibiotic efficacy in rats infected with antibiotic-resistant bacteria," Ann NY Acad Sci 797: 285-287; Oct 1996. **Direct Quote:** "Results of these studies demonstrated that prophylaxis with PGG glucan in combination with antibiotics provided enhanced protection against lethal challenge with Escherichia coli or Staphylococcus aureus as compared with the use of antibiotics alone."

Free Radical Scavenger:

Sener G, Eksioglu-Demiraop E, Cetiner M, Ercan F, Yegen BC; "beta-glucan ameliorates methotrexate-induced oxidative organ injury via its antioxidant and immunomodulatory effects." European J Pharmacology; 542(1-3):170-178; Epub May 2006. Aug 7 2006. **Direct Quote:** **"Methotrexate is an antifolate [antimetabolite chemotherapy drug] that is widely used in the treatment of rheumatic disorders and malignant tumors. The efficacy of methotrexate is often limited by severe side effects and toxic sequelae [disease condition caused by a disease], where oxidative stress [free radical damage] is noticeable. ... Thus, the findings of the present study suggest that beta-glucan, through its antioxidant and immunoregulatory effects, may be of therapeutic value in alleviating the leukocyte apoptosis [white immune cell death], oxidative [free radical] tissue injury and thereby the intestinal and hepatorenal [liver or kidney] side effects of methotrexate treatment."**

Carrow, D.J.; "Beta-1,3-glucan as a Primary Immune Activator," Townsend Letter; June 1996. **Direct Quote:** **"Free radical scavenging assays were repeated in different models, which then confirmed the antioxidant effect of beta 1,3-glucan. In light of what is presently known about the potential of free radicals to accelerate aging, cause cancer and other degenerative diseases, this particular effect of beta 1,3-glucan is especially important."**

Sener G, Toklu H, et al; "Protective effect of beta-glucan against oxidative organ injury in a rat model of sepsis," Int Immunopharmacol:1387-96 Epub 2005/Aug 2005. **Direct Quote:** **"Sepsis leads to various organ damage and dysfunction. One of the underlying mechanisms is thought to be oxidative damage due to generation of free radicals. ...Elevated plasma TNF-alpha levels in septic rats [was] significantly reduced to control levels in beta-glucan treated rats. Since beta-glucan administration reversed these oxidant responses, it seems likely that beta-glucan protects against sepsis-induced oxidative organ injury."**

Fungal Diseases and Pathogens:

Hunter KW, Jr. Berner MD, Sura ME Alvea BN, "IFN-gamma primes macrophages for enhanced TNF-alpha expression in response to stimulatory and non-stimulatory amounts of microparticulate beta-glucan.," **Immunol Lett ; 15:98(1): 115-22.** Department of Microbiology and Immunology, University of Nevada School of Medicine, Applied Research Facility, MS-199, Reno, NV 89557, USA. April 2005, **Direct Quote:** **... "we have tested a new microparticulate form of beta-(1--> 3)-D-glucan (MG) from Saccharomyces cerevisiae for its ability to induce proinflammatory cytokine secretion in mouse peritoneal macrophages in vitro, and we have examined the effect of IFN-gamma. MG was rapidly phagocytized by peritoneal macrophages, and these MG-treated macrophages upregulated TNF-alpha, IL-6, and IL-1beta mRNAs and secreted these proinflammatory cytokines. These data suggest that a synergy between IFN-gamma and beta-glucan may have evolved to lower the threshold of sensitivity of the innate immune response to fungal pathogens."** [respond faster in attacking fungal pathogens – mycotoxins]

Pelizon AC, Kaneno R, et al; "Immunomodulatory activities associated with beta-glucan derived from Saccharomyces cerevisiae." Dept of Microbiology and Immunology, Inst of Biosciences, State U of Sao Paulo Brazil. Physio Res. 54(5):557-64 2005. **Direct Quote:** **"B-glucan enhances fungicidal activity against P. brasiliensis...B-glucan primes for higher IL12 and TNF-alpha production....B-glucan increases NK [Natural Killer white immune cells]. ...The lower dose [20 mg/ml] was more effective to increase NK and fungicidal activity....Together, our results suggest that B-glucan**

derived from S. cerevisiae is able to improve Immune functions that contribute to P. brasiliensis elimination

Browder IW., Williams D., Pretus H., et al; *Beneficial Effect of Enhanced Macrophage Function in the Trauma Patients*. Ann. Surg.; Vol 211: 605-613. Dept of Surg and Physiol, Tulane U Sch of Med, LA and Istituto Di Chirurgia D'Urgenza, U of Torino, Torino, Italy.* 1990. **Direct Quote:** ***“Previous studies have demonstrated that glucan, a beta-1,3-linked glucopyranose polymer, isolated from the inner cell wall of Saccharomyces cerevisiae, is a potent macrophage stimulant and is beneficial in the therapy of experimental bacterial, viral, and fungal diseases.”***

Jamas S, Easson D, Ostroff G: *“Underivatized aqueous soluble beta (1,3) glucan, composition and method of making same.”* U.S. Patent Application 20020032170, March 14, 2002. **Direct Quote:** ***“The use of soluble and insoluble beta glucans alone or as vaccine adjuvants for viral and bacterial antigens has been shown in animal models to markedly increase resistance to a variety of bacterial, fungal, protozoan and viral infections.”***

DiLuzio N.R., *“Immunopharmacology of glucan: a broad spectrum enhancer of host defense mechanisms,”* Trends in Pharmacol. SCI., 4:344-347. Dept of Physiology, Tulane U, New Orleans, LA 1983. **Direct Quote:** (p347) ***“The broad spectrum of immunopharmacological activities of glucan includes not only the modification of certain bacterial, fungal, viral and parasitic infections, but also inhibition of tumor growth.”***

Williams D.L., Browder I. and DiLuzio N.R., *“Soluble phosphorylated glucan: methods and compositions for wound healing,”* U.S. Patent 4975421, Issued Dec 4, 1990. **Direct Quote:** ***“The soluble phosphorylated glucans are useful for promoting the wound healing process. The soluble phosphorylated glucans are also useful for prophylactic and therapeutic applications against neoplastic, bacteria, viral, fungal and parasitic diseases.”***

Heart - Coronary Artery Disease:

Robert Nicolosi, Stacey J Bell, Bruce R Bistrain, Isaac Greenberg, R Armour Forse and George L Blackburn, *“Cholesterol Benefits from Beta 1,3/1,6 Glucan Purified from Yeast Cell Wall,”* Nutrition and Infection Laboratory, Harvard Medical School; the Centers for the Study of Nutrition and Medicine and for Nutritional Research, and Clowes Surgical Metabolism Laboratory, Beth Israel Deaconess Medical Center, Boston. American Journal of Clinical Nutrition, Vol. 70, No. 2, 208-212, August 1999. **Direct Quote:** ***“The purpose of this study was to evaluate the effect on serum lipids of a yeast-derived β -glucan fiber in 15 free-living, obese, hypercholesterolemic men. ... The yeast-derived β -glucan fiber significantly lowered total cholesterol concentrations and was well tolerated...The link between elevated plasma LDL-cholesterol concentrations and the risk of developing coronary artery disease has been clearly established...Elevated plasma cholesterol and, in particular, LDL-cholesterol concentrations are associated with increased risk of coronary artery disease, whereas an elevated of HDL-cholesterol concentration is inversely correlated with the incidence of cardiovascular... The yeast-derived β -glucan fiber lowered total cholesterol and raised HDL-cholesterol concentrations significantly. ... Unlike the significant increases in HDL-cholesterol concentrations observed 4 wk after the end of the study for subjects receiving the yeast-derived β -glucan, none of the 24 studies of oat products reported significant changes in HDL concentration. ... Because higher HDL-cholesterol concentrations are associated with a reduced risk of developing coronary artery disease, there may be unique benefits of using the yeast-derived β -glucan, and perhaps psyllium, rather than the oat products.”***

Carrow, D.J.; "Beta-1,3-glucan as a Primary Immune Activator," Townsend Letter; June 1996. **Direct Quote:** "...immunosuppression is observed in people with stress-related disease such as coronary heart disease. Under such influences the number of macrophages [white immune cells] available are reduced and unable to participate in the immune cascade, which caused an even greater immunosuppression. Beta 1,3 glucan has proven to both stimulate and activate the macrophage cells, which will counter these negative effects. ...People with high risk of atherosclerosis should definitely add beta 1,3 glucan to their diet in addition to any cholesterol-reducing drugs. Macrophage activation helps draw extra cholesterol from the blood, prevent further plaque formation on the arterial walls and phagocytes [eats] existing plaque which is recognized as a foreign body."

Hemopoietic (or hematopoietic) Recovery – Formation of Blood Cells:

Daniel E Cramer, Daniel J Allendorf, Jarek T Baran, Richard Hansen, Jose Marroquin, Bing Li, Janina Ratajczak, Mariusz Z Ratajczak, and Jun Yan "Beta-glucan enhances complement-mediated hematopoietic recovery after bone marrow injury," Blood; DOI 10.1182. Tumor Immunobiology Program and Stem Cell Biology Program, James Graham Brown Cancer Center, University of Louisville, Louisville, KY, USA. Sept 2005. **Direct Quote:** "...Myelotoxic injury in the bone marrow (BM) as a consequence of total body irradiation (TBI) or granulocyte colony stimulating factor (G-CSF) mobilization results in the deposition of iC3b on BM [bone marrow] stroma [cell framework]. ... Taken together, these observations suggest a novel role for C, CR3, and Beta glucan in the restoration of hematopoiesis following injury." NOTE: Mice were treated for 12 days with beta glucan and exposed to a sublethal dose of radiation. The beta glucan treated animals had approximately 40 percent more cell formation units in the spleen than untreated mice. When beta glucan was given orally, survival of animals receiving a lethal dose of radiation after stem cell transplantation was significantly enhanced. Forty days following radiation exposure, approximately 30 percent of mice treated with beta glucan survived compared with only 3 percent of untreated animals.

Patchen M.L., McVittie T.J.; *Temporal Response of Murine Pluripotent Stem Cells and Myeloid and Erythroid Progenitor Cells to Low-dose Glucan Treatment.* Acta Hemat; 70:281-288. Experimental Hematology Dept, Armed Forces Radiobiology Research Insti, Bethesda, MD. 1983. **Direct Quote:** "Clearly, there are numerous possible uses for an agent such as glucan, which is a potent stimulator of hemopoietic activity. Currently, we [U.S. Armed Services] are using glucan to enhance hemopoietic proliferation in conjunction with hemopoietic injury induced by radiation."

Hepatitis – Viral :

Williams D.L. and DiLuzio N.R.; "Glucan-Induced Modification of murine Viral Hepatitis". Science (1980), 208: 67-69. 1980. **Direct Quote:** "Thus glucan is capable of increasing survival, inhibiting hepatic necrosis, and maintaining an activated state of phagocytic activity in mice challenged with [mouse hepatitis virus strain] MHV-A59."

IL 1 and TNF Alpha Production:

Hunter KW, Jr. Berner MD, Sura ME Alvea BN, "IFN-gamma primes macrophages for enhanced TNF-alpha expression in response to stimulatory and non-stimulatory amounts of microparticulate beta-glucan.," **Immunol Lett** ; **15:98(1): 115-22**. Department of Microbiology and Immunology, University of Nevada School of Medicine, Applied Research Facility, MS-199, Reno, NV 89557, USA. April 2005, **Direct Quote:** *... "we have tested a new microparticulate form of beta-(1--> 3)-D-glucan (MG) from Saccharomyces cerevisiae for its ability to induce proinflammatory cytokine secretion in mouse peritoneal macrophages in vitro, and we have examined the effect of IFN-gamma. MG was rapidly phagocytized by peritoneal macrophages, and these MG-treated macrophages upregulated TNF-alpha, IL-6, and IL-1beta mRNAs and secreted these proinflammatory cytokines. These data suggest that a synergy between IFN-gamma and beta-glucan may have evolved to lower the threshold of sensitivity of the innate immune response to fungal pathogens." [respond faster in attacking fungal pathogens – mycotoxins]*

Immune Response Potentiation:

Hunter K, Gault R, Jordan F, "Mode of Action of B-Glucan Immunopotentiators," Department of Microbiology, University of Nevada School of Medicine, Oct 1998. **Direct Quote:** *"... the size of a particle is one factor influencing phagocytic [microbe ingestion] efficiency by macrophages. ...the number of macrophages actively phagocytosing [ingesting microbes] is affected by the particle size of the glucan. This would suggest that, in vivo, a greater number of macrophages may be activated and thus would provide an enhanced immune response. ...these data do indicate that glucan particle size is an important factor in the production of nitric oxide. Nitric oxide is generated during the "oxidative burst" that kills ingested microbes. This would suggest that the small particle glucan [MG Glucan] has greater ability to enhance the immune system than the globular form of glucan."*

Jordan F, Hunter Jr. KW, Gault R, "Method for preparing small particle size glucan in a dry material," U.S. Patent 6,476,003. November 2002.

Direct Quote: *"The greater generation and/or production of NO (Nitric Oxide) demonstrates the enhanced activity of the macrophage with a small particle size glucan which is indicative of an activity level of an immune system. ... The measurement of NO production is indicative of an oxidative burst that kills and/or destroys the ingested microbes and/or particles by the macrophage. As a glucan re-aggregates into particles of greater than one micron in diameter, it appears to pass through an animal or human digestive system without substantially complete absorption. As the glucan re-aggregates to a size of greater than one micron in diameter, some of the beneficial effect of the glucan is not achieved because the macrophage receptors are not activated as readily by glucan greater than one micron in diameter because the receptor size on corresponding cells and molecules that accept the glucan is generally about one micron in size. ...The greater percentage phagocytosis demonstrates the enhanced activity of the macrophage and the small particle size glucan's ability to activate the immune system."*

Hunter KW, Gault RA, Berner MD, "Preparation of microparticulate B-glucan from Saccharomyces cerevisiae for use in immune potentiation." Letters in Applied Microbiology," Vol 35 Issue 4, 267-271, October 2002 .

Janusz M.J., Austen K.F., Czop J.K.; "Isolation of a Yeast Heptaglycoside that Inhibits Monocyte Phagocytosis of Zymosan Particles". The Journal of Immunology; 142:959-965. Dept of Med, Harvard Med Sch, Boston, MA 1989. **Direct Quote:** *"Beta-Glucans with 1,3-and 1,6 glycosidic linkages are the*

major structural components of yeast and fungal cell walls and are active pharmacologic agents in host defense systems of plants and animals....The administration of particulate glucans from S. cerevisiae to laboratory animals induces host resistance to a variety of lethal pathogens by mechanisms involving macrophage stimulation."

Immune Response – Macrophage Cell Production Increase:

Burgaleta C., Territo M.C., Quan C.G., Goide D.W.; *Glucan activated macrophages: functional characteristics and surface morphology*; J Reticuloendothel Soc 23: 195-204. 1978. **Direct Quote:** *"These studies indicate that glucan administration results in increased granulocyte and macrophage production....glucan as an immunotherapeutic agent can result in an increased number of available effector cells."*

Ishibashi K, Miura NN, et al, "Relationship between the physical properties of Candida albicans cell wall beta-glucan and activation of leukocytes in vitro," Int Immunopharmacol 2(8):1109-22. Jul 2002. **Direct Quote:** *"Beta-glucan activated leukocytes significantly more effectively in a particulate than solubilized form in terms of TNF-alpha production by RAW 264.7 cells, hydrogen peroxide production by murine PEC and IL-8 production by human PBMC....These facts strongly suggested that the solubility and assembly of the components influence the immunopharmacological activities of 1,3-beta-D-glucans."*

Immune Response – Potentiation:

Czop, J.K., Valiante N.M., Janusz M.J.; "Phagocytosis of particulate activators of the human alternative complement pathway through monocyte beta-glucan receptors," Prog Clin Biol Res 297: 287-296; Dept of Med, Harvard Med S, Boston, MA. 1989. **Direct Quote (p1):** *"Animal studies indicate that beta-glucans with 1,3-and/or 1,6-linkages are active pharmacologic agents that rapidly confer protection to a normal host against a variety of biological insults. The beta-glucan receptors provide a mechanism by which a heightened state of host responsiveness is initiated."*

Immune Response – Small Particle Effectiveness:

Hunter KW, Gault RA, Berner MD, "Preparation of microparticulate B-glucan from Saccharomyces cerevisiae for use in immune potentiation." Letters in Applied Microbiology," Vol 35 Issue 4, 267-271, October 2002

Direct Quote: *"...there was evidence that macrophages, key target cells for the immunopharmacological activity of B-glucans, preferentially ingest particles in the 1-2-µ (micron) diameter size range." "Compared with the aggregated form of B-glucan, the B-glucan microparticles ... are more effective at enhancing phagocytosis by peritoneal macrophages following oral administration. Although both aggregated [5-100-µ micron diameter] and microparticulate [1-2-µ micron diameter] glucans enhanced peritoneal macrophage activation when administered orally in mice, the microparticulate glucan was significantly better than the aggregated form."*

Hunter K, Gault R, Jordan F, "Mode of Action of B-Glucan Immunopotentiators," Department of Microbiology, University of Nevada School of Medicine, Oct 1998.

	Globular Glucan	Sonicated Microparticulate Glucan (µg/ml)	Media
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	(µg/ml)		
Nitric Oxide (µM)	275	600	0

Direct Quote: "...this data does indicate Glucan particle size is an important factor in the production of nitric oxide. Nitric oxide is generated during the "oxidative burst" that kills ingested microbes [bacteria, viruses, fungi, parasites, etc]. This would suggest that the small particle glucan has greater ability to enhance the immune system than the globular form of glucan."

Donzis B. A.; "Substantially purified beta (1,3) finely ground yeast cell wall glucan composition with dermatological and nutritional uses;" U.S. Patent 5702719; 1997. **Direct Quote:** "The preferred particle size of the fine grind glucan product is about 1.0 micron or less and more preferably, .20 microns or less."

Donzis B. A.; "Substantially purified beta (1,3) finely ground yeast cell wall glucan composition with dermatological and nutritional uses;" U.S. Patent 5576015; 1996. **Direct Quote:** "Upon oral administration, the smaller or finer particle sized glucan is more quickly dissolved in the gastrointestinal tract and consequently, more readily absorbed."

Immune Response Enhancement: - Oral Applications:

Janusz M.J., Austen K.F., Czop J.K.; "Lysosomal enzyme release from human monocytes by particulate activators is mediated by beta-glucan inhibitable receptors," J. Immunol 138: 3897-3901. 1987. **Direct Quote:** "This demonstration of bactericidal enhancement via oral dosing suggests an application for beta-1,3-glucan as a component in a combined modality with conventional anti-infective agents. Beta glucan, through the stimulation of host defense systems, creates a more supportive environment within the body to assist the primary killing action of the conventional agent."

Kimura A., et al., "In Vitro Activation of Human Adherent Cells by a Glucan, Schizophyllan". J. Reticuloendothel.; Soc. 34: 1-11. 1983. **Direct Quote:** "...Glucan-treated rats had significantly increased rates of phagocytosis and killing of Staphylococcus aureus immediately after infection..."

Meira, D.A., et al; *The Use of Glucan as Immunostimulant in the Treatment of Paracoccidioidomycosis*; Am J. Trop Med Hyg 55(5), 496-503; 1996. Dept of Trop Dis, Dept of Microbio, State U of Sao Paulo, Brazil. **Direct Quote:** "...glucan enhances the immune response through stimulation of macrophages by increasing their number, size, and function, stimulates secretion of lysozyme and TNF by activated macrophages, increases the phagocytosis of antigens, activates the formation of granulocyte and monocyte colonies, and factors increased activity of T and B lymphocytes, as well as complement activation."

Poutsika D.D., et al, "Cross-linking of the beta-glucan receptor on human monocytes results in interleukin-1 receptor antagonist but not interleukin-1 production," Blood 82: 3695-3700 ; 1993. Dept of Med, New England Med Ctr, Boston, MA. **Direct Quote:** "Because of their differential effects on cytokine production, beta-glucans may be used to therapeutic advantage in the diseases in which IL-1 is implicated."

Bousquet M., Escoula L. et al; "Immunopharmacologic study in mice of 2 beta-1,3, beta-1,6 polysaccharides (scleroglucan and PSAT) on the activation of macrophages and T lymphocytes," Ann Rech Vet 20: 165-173. 1989. Station of Pharmacologie-Toxicologie, INRA, Toulouse, France. **Direct Quote:** "...PSAT and

scleroglucan favorably affect the non-specific host defense and cellular immune response in mice."

Impaired Immunity:

Carrow, D.J. M.D.; "Beta-1,3-glucan as a Primary Immune Activator," Townsend Letter; June 1996. **Direct Quote:** *"The following list includes benefits from the use of Beta 1,3-glucan supplementation: People who have impaired immunity from any cause including, but not limited to HIV infection; have a high occurrence of infectious diseases; have tumors and/or those undergoing chemotherapy or radiation therapy; are over forty who are concerned about the natural aging process or might have noticed a slowing down of immune reactivity; who are geriatric patients; and other with compromised immune disorders."* *In vitro studies reveal that bone marrow-derived mouse macrophages and human peripheral blood monocytes possess Beta-glucan receptors that mediate phagocytosis of glucan particles and induce release of proinflammatory mediators..."*

Infection:

Hunter K, Gault R, Jordan F, "Mode of Action of B-Glucan Immunopotentiators-Research Summary Release," Department of Microbiology, University of Nevada School of Medicine, Jan 2001. **Direct Quote:** *Glucan has been shown to enhance the envelopment and digestion (phagocytosis) of pathogenic microorganisms that cause infectious disease...Laboratory studies have revealed the new MG Glucan is significantly effective at activating Macrophages, and via the Macrophages, the entire immune cascade including T-Cells and B-Cells."*

Infection - Intrauterine:

Singh U, Nicholson G, et al; "Immunological properties of human decidual macrophages - a possible role in intrauterine immunity," *Reproduction*;129(5):631-7, Nuffield Dept. of Obstetrics and Gynaecology, U of Oxford, UK; May 2005.

Direct Quote: *"These results suggest a role for decidual (uterine mucous wall) macrophages in pathogen recognition and clearance during pregnancy, and, therefore, they are likely to protect the fetus against intrauterine infections which might otherwise lead to preterm labour."* Note: Beta 1,3/1,6-d glucan potentiates the macrophage immune cells and is referenced in the complete study.

Infections - Secondary:

Gu YH, Takagi Y, et al; "Enhancement of radioprotection and anti-tumor immunity by yeast-derived beta-glucan in mice," *J Med Food*. 8(2) 154-8; Dept of Radiological Technology, Suzuka U of Med Sc, Suzuka, Japan, Summer 2005. **Direct Quote:** *"Intraperitoneal injection of beta-glucan was shown to greatly delay mortality in mice exposed to whole-body X-ray radiation and tumor growth in tumor-bearing mice. ...Augmented immunological activity as seen in increased NK (natural killer) and LAK (lymphokine-activated killer) activity by beta-glucan seems to play a role in preventing secondary infections associated with irradiation and probably contributes to the attenuated [reduced] tumor growth in tumor-bearing mice through enhanced anti-tumour immunity. These results suggest that beta-glucan may be a promising adjunct treatment for cancer patients receiving radiotherapy."*

Infections: General:

Jamas S, Easson D, Ostroff G: "Underivatized aqueous soluble beta (1,3) glucan, composition and method

of making same." U.S. Patent Application 20020032170, March 14, 2002. **Direct Quote:** *"The use of soluble and insoluble beta glucans alone or as vaccine adjuvants for viral and bacterial antigens has been shown in animal models to markedly increase resistance to a variety of bacterial, fungal, protozoan and viral infections."*

Infection – Abdominal:

Bowers GJ, Patchen ML, et al, "Glucan enhances survival in an intraabdominal infection model," J Surg Res 47(2): 183-188; Aug 1989

Infection-M bovis,BCG:

Hetland G, Wiker H, "Protective effect of beta-glucan against mycobacterium bovis, BCG infection in BALB/c mice." Scand J Immunol, 47:6, 548-53, Jun 1998. **Direct Quote:** *"Beta 1,3-glucan is a potent stimulator of macrophage functions and has a protective effect against a range of infections in rodent models."*

Infection - Escherichia coli :

Onderdonk, A.B., et al., "Anti-Infective Effect of Poly-.beta.1-6 -Glucotrisyl-.beta.1-3-Glucopyranose Glucan In Vivo," Infec. Immun.; 60:1642-1647. 1992. Dept of Pathology, Channing Lab, Brigham and Women's Hospital, Boston, MA.

Direct Quote: *"Mice challenged with Escherichia coli or Staphylococcus aureus were protected against lethal peritonitis by the intravenous administration of 10 micrograms of poly-beta 1-6-glucotriosyl-beta 1-3-gluco-pyranose (PGG) glucan per animal 4 to 6 h prior to bacterial challenge."*

Browder IW.,et al., "Protective Effect of Nonspecific Immunostimulation in Post Splenectomy Sepsis". J. Surg. Res.; 35: 474-479. Dept of Surg and Physiol, Tulane U Sch of Med, LA. 1983. **Direct Quote:** *"This study reports the use of glucan, a beta-1,3-polyclucose, as a nonspecific immunostimulant for postsplenectomy pneumococcal sepsis. ...Nonspecific immunostimulation appears to have significant potential as a treatment strategy against postsplenectomy infection."*

Maurici da Rocha e Silva et al; "Infection Prevention in Patients with Severe Multiple Trauma with the Immunomodulator Beta 1-3 Polyglucose (glucan);" Surgery, Gynecology & Obstetrics; 177:383-388. 1993.

Direct Quote: *"The incidence of hospital pneumonia of 55% and sepsis of 35% confirms results of previous studies of patients with multitrauma. Glucan decreased pneumonia and sepsis to a significantly lower level of 9.5%....The mortality rate related to infection decreased from 30.0 to 4.8%. The lower number of instances of pneumonia and sepsis....decreased the period of time in the intensive care and the hospital, with a global reduction of 40% on hospital cost."*

Infection - Staphylococcus Aureus :

DiLuzio N.R., Williams DL; "Enhancement of host susceptibility to Staphylococcus aureus infection by chronic ethanol ingestion—modification by glucan immunostimulation," Alcohol Clin Exp Res 4(3): 254-260. Jul 1980. **Direct Quote:** "*The administration of glucan significantly prolonged survival of S. Aureus infected control and chronic ethanol mice.*"

Kimura A., et al., "In Vitro Activation of Human Adherent Cells by a Glucan, Schizophyllan". J. Reticuloendothel.; Soc. 34: 1-11. 1983. **Direct Quote:** "*...Glucan-treated rats had significantly increased rates of phagocytosis and killing of Staphylococcus aureus immediately after infection...*"

DiLuzio N.R. and Williams D.L., "Glucan-Induced Modification of the Increases Susceptibility of Cyclophosphamide-Treated Mice to Staphylococcus aureus Infection". Cancer Immunol. Immunother.; 6: 73-79. 1979.

DiLuzio N.R., Williams D.L., et al, "Comparative tumor-inhibitory and anti-bacterial activity of soluble and particulate glucan," Int J Cancer, 24(6):773-779. Dec 1979. **Direct Quote:** "*...these studies demonstrate that a soluble glucan preparation exhibits significant anti-tumor and anti-staphylococcal activity.*"

Dernodle D, Gates H, Kaiser A, "Prophylactic anti-infective activity of poly-[1,6]-beta-D-glucopyranosyl-[1,3]-beta-D-glucopyranose glucan in a guinea pig model of staphylococcal wound infection," Antimicrob Agents Chemother, 42:3,545-9. Mar 1998. **Direct Quote:** "*...glucan reduces the risk of staphylococcal abscess formation. Neutrophil-activating agents [glucan] are a novel means of prophylaxis against surgical infection and may be less likely than antibiotics to be affected adversely by the increasing antibiotic resistance of nosocomial pathogens.*"

I. P.W.A., et al., Activation of the Alternative Complement Pathway by Water-Insoluble Glucans of Streptococcus mutans: the Relation Between Their Chemical Structures and Activating Potencies". Macrophage-Mediated Destruction of Human Malignant Cells In Vitro; Inai et al., J. Immunol (1976); 1256-1260. 1976.

Babineau, et al., "Randomized Phase I/II Trial of a Macrophage-Specific Immunomodulator (PGG-Glucan) in High Risk Surgical Patients", Annals of Surgery; 220:(5):601-609. 1994. Dept of Surgery, Deaconess Hospital, Harvard Medical Sch, Boston MA **Direct Quote:** "*PGG-glucan is safe and appears to be effective in further reduction of the morbidity and cost of major surgery.*"*

Kokoshis P.L., Williams D.L., Cook J.A., Di Luzio N.R.; Increased resistance to Staphylococcus aureus infection and enhancement in serum lysozyme activity by glucan. Science 199: 1340-1342, 1978. **Direct Quote:** "*These studies indicate that glucan confers an enhanced state of host defense against bacterial infections.*"

* Rasmussen, LT and Seljelid, R.: "Novel Immunomodulators With Pronounced In Vitro Effects Caused by Stimulation of Cytokine Release", Journal of Cellular Biochemistry; 46:60-68. Inst of Med Bio, U of Tromso, Norway. 1991. **Direct Quote:** "*Beta-1,3-D-polyglucose derivatives protect mice against otherwise lethal bacterial infections.*"

Glovsky MM, et al.; "Effects of particulate beta-1,3 glucan on human, rat, and guinea pig complement activity," J. Reticuloendothel Soc. 33:401-413. 1983. **Direct Quote:** "*Glucan administration is associated with the modification of a variety of experimentally induced infectious disease states as well as the inhibition of growth of implantable and spontaneous tumors.*"

Infections – Surgical Procedures:

Norton MD, JA [Prof of Surg, Chief of Endocrine and Oncologic Surgery]; “*Editorial: Annals of Surgery,*” Washington University School of Medicine, Nov 1994. **Direct Quote:** “*In a prospective, randomized double-blind study, [Babineau, et.al.] demonstrate that the perioperative administration of PGG-glucan, a substance derived from yeast that increases the microbial killing activity of leukocytes, can decrease infectious complications in patients undergoing major surgical procedures...the preliminary results are positive and should be interpreted as good news.*”

Injury (from irradiation):

Daniel E Cramer, Daniel J Allendorf, Jarek T Baran, Richard Hansen, Jose Marroquin, Bing Li, Janina Ratajczak, Mariusz Z Ratajczak, and Jun Yan “*Beta-glucan enhances complement-mediated hematopoietic recovery after bone marrow injury,*” Blood; DOI 10.1182. Tumor Immunobiology Program and Stem Cell Biology Program, James Graham Brown Cancer Center, University of Louisville, Louisville, KY, USA. Sept 2005. **Direct Quote:** “*...Myelotoxic injury in the bone marrow (BM) as a consequence of total body irradiation (TBI) or granulocyte colony stimulating factor (G-CSF) mobilization results in the deposition of iC3b on BM [bone marrow] stroma [cell framework]. ... Taken together, these observations suggest a novel role for C, CR3, and Beta glucan in the restoration of hematopoiesis [cell formation] following injury.*” NOTE: Mice were treated for 12 days with beta glucan and exposed to a sublethal dose of radiation. The beta glucan treated animals had approximately 40 percent more cell formation units in the spleen than untreated mice. When beta glucan was given orally, survival of animals receiving a lethal dose of radiation after stem cell transplantation was significantly enhanced. Forty days following radiation exposure, approximately 30 percent of mice treated with beta glucan survived compared with only 3 percent of untreated animals.

Leukemia:

DiLuzio NR, Williams DL, “*Protective effect of glucan against systemic Staphylococcus aureus septicemia in normal and leukemic mice,*” Infect Immun 20(3):804-810. Dept of Physiology, Tulane U, New Orleans, LA. Jun 1978. **Direct Quote:** “*These data denote that glucan enhances nonspecific resistance to S. aureus sepsis, promotes survival during leukemic episodes, and increases survival time of leukemic mice with experimentally induced:*

Stewart C.C., et al., “*Preliminary Observations on the Effect of Glucan in Combination with Radiation and Chemotherapy in Four Murine Tumors,*” Cancer Treat. Prep.; 62: 1867-72. 1978. **Direct Quote:** “*The efficacy of glucan in combination with BCNU chemotherapy was measured using the disseminated AKR transplantable leukemia; the combination yielded a high level of cures compared to no survival for either agent alone.*”

Williams D.L, DiLuzio NR, “*Glucan induced modification of experimental Staphylococcus aureus infection in normal, leukemic and immunosuppressed mice.*” Adv Exp Med Biol 121(A):291-306. 1979 **Direct Quote:** “*...A post-treatment regimen of glucan significantly enhanced survival of AKR/J mice with lymphocytic leukemia as well as leukemic mice with experimentally induced systemic staphylococcal infection.*”

Lipid Metabolism Disorder:

Pola P, "Composition for the prevention and/or treatment of lipid metabolism disorders and allergic forms," U.S. Patent Application 20030017999, January 23, 2003. **Direct Quote:** ".beta-1,3-D-glucan has proved effective not only in preventing lipid metabolism disorders, but also in stimulating immune defenses, in preventing onset of tumors and in controlling serum glucose."

Liver Damage:

Sener G, Eksioglu-Demiraop E, Cetiner M, Ercan F, Yegen BC; "beta-glucan ameliorates methotrexate-induced oxidative organ injury via its antioxidant and immunomodulatory effects." European J Pharmacology; 542(1-3):170-178; Epub May 2006. Aug 7 2006. **Direct Quote:** "**Methotrexate is an antifolate [antimetabolite chemotherapy drug] that is widely used in the treatment of rheumatic disorders and malignant tumors. The efficacy of methotrexate is often limited by severe side effects and toxic sequelae [disease condition caused by a disease], where oxidative stress [free radical damage] is noticeable. ... Thus, the findings of the present study suggest that beta-glucan, through its antioxidant and immunoregulatory effects, may be of therapeutic value in alleviating the leukocyte apoptosis [white immune cell death], oxidative [free radical] tissue injury and thereby the intestinal and hepatorenal [liver or kidney] side effects of methotrexate treatment.**"

Toklu HZ, Sehirili AO, Velioglu-Ogunc A, Centinel S, Sener G; "Acetaminophen-induced toxicity is prevented by beta-d-glucan treatment in mice." European J Pharmacology; 543(1-3):133-40; Epub 2006 Jun; Jun 2, 2006.

Direct Quote: "**The protective effect of beta-glucan against oxidative injury caused by acetaminophen [Tylenol, Anacin 3, Tempra, Datriil] was studied in mice liver...Acetaminophen caused a significant decrease in the GSH level of the tissue, which was accompanied with significant increases in the hepatic luminol and lucigenin chemiluminescence values, malondialdehyde level, MPO activity and collagen content. Similarly, serum ALT, AST levels, as well as LDH and TNF-alpha, were elevated in the acetaminophen-treated group...beta-d-glucan treatment reversed all of these [liver toxicity] biochemical indices, as well as histopathological alterations that were induced by acetaminophen. In conclusion, these results suggest that beta-d-glucan exerts cytoprotective effects against oxidative injury through its antioxidant properties and may be of therapeutic use in preventing acetaminophen toxicity.**"

Lung Damage - Sepsis:

Babayigit H, Kucuk C, Sozuer E, Yazici C, Kose K, Akgun H.; "Protective effect of beta-glucan on lung injury after cecal ligation and puncture in rats." Department of General Surgery, School of Medicine, Erciyes University, 38039, Kayseri, Turkey; Intensive Care Med. (6):865-70; Jun 31, 2005. **Direct Quote:** "**In this rat model of intra-abdominal sepsis beta-glucan treatment partially protected against secondary lung injury, decreased lung hemorrhages, and lung neutrophilia. These results suggest that beta-glucan protects against sepsis-associated lung damage.**"

Macrophage Activation:

Abel G. and Czop, J.K., "Stimulation of human monocyte beta-glucan receptors by glucan particles induces production of TNF-alpha and IL-1 beta," Int. J. Immunopharmacol, 14:; 1363-1373. 1992.

Abel, G. and Czop, J.K., "Activation of Human Monocyte GM-CSF and TNF-. alpha. Production by Particulate Yeast Glucan," International Congress for Infectious Diseases, Montreal, Canada (abstract). 1990.*

Adachi Y., Ohno N., Ohsawa M., Oikawa S., Yacomae T.; "Macrophage activation in vitro by chemically cross-linked (1--3)-beta-D-glucans," Chem Pharm bull (Tokyo), 38:988-992 1990. Laboratory of Immunopharmacology of Microbial Products, Tokyo College of Pharmacy, Japan.*

Suzuki I, Tanaka H, Kinoshita A, Oikawa S, Osawa M, Yadomae T, "Effect of orally administered beta-glucan on macrophage function in mice," Int J Immunopharmacol, 12(6)675-684. 1990. **Direct Quote:** "These results demonstrate that SSG [beta 1,3 glucan] given by the oral route can activate peritoneal macrophages in mice."

Melanoma:

Williams DL, et al, "Therapeutic efficacy of glucan in a murine model of hepatic metastatic disease," Hepatology 5(2):198-206. Mar 1985. **Direct Quote:** "...coincubation of particulate glucan with diverse populations of normal or tumor cells in vitro indicated that glucan exerted a direct cytostatic effect on sarcoma and melanoma cells and, in contrast, had a proliferative effect on normal spleen and bone marrow cells."

Methotrexate:

Sener G, Eksioglu-Demiraop E, Cetiner M, Ercan F, Yegen BC; "beta-glucan ameliorates methotrexate-induced oxidative organ injury via its antioxidant and immunomodulatory effects." European J Pharmacology; 542(1-3):170-178; Epub May 2006. Aug 7 2006. **Direct Quote:** "Methotrexate is an antifolate that is widely used in the treatment of rheumatic disorders and malignant tumors. The efficacy of methotrexate is often limited by severe side effects and toxic sequelae [disease condition caused by a disease], where oxidative stress is noticeable. ... Thus, the findings of the present study suggest that beta-glucan, through its antioxidant and immunoregulatory effects, may be of therapeutic value in alleviating the leukocyte apoptosis [white immune cell death], oxidative tissue injury and thereby the intestinal and hepatorenal [liver or kidney] side effects of methotrexate treatment."

Microbes:

Lablanc BW, Albina JE, Reichner JS, "The effect of PGG-{beta}-glucan on neutrophil chemotaxis in vivo." Dept of Surgery, Rhode Isl Hospital and Brown Med Sch. Providence. J Leukoc Biol Jan 13, 2006. **Direct Quote:** "The beta-glucans are long-chain polymers of glucose in beta-(1,3)(1,6) linkages, which comprise the fungal cell wall and stimulate cells of the innate immune system. ...Taken together, these findings demonstrate that beta-glucan directly affects the chemotactic capacity of circulating neutrophils...and potentiates antimicrobial host defense."

Brown GD, Gordon S; "Immune recognition. A new receptor for beta-glucans." Sir William Dunn School of Pathology, University of Oxford, Nature 6;413(6851):36-7. Sep 2001. **Direct Quote:** "The carbohydrate polymers known as beta-1,3-d-glucans exert potent effects on the immune system - stimulating antitumour and antimicrobial activity, for example - by binding to receptors on macrophages and other white blood cells and activating them."

Mycotoxins:

Hunter KW, Jr. Berner MD, Sura ME Alvea BN, "IFN-gamma primes macrophages for enhanced TNF-alpha expression in response to stimulatory and non-stimulatory amounts of microparticulate beta-glucan."

Immunol Lett ; 15:98(1): 115-22. Department of Microbiology and Immunology, University of Nevada School of Medicine, Applied Research Facility, MS-199, Reno, NV 89557, USA. April 2005, **Direct Quote:** *... "we have tested a new microparticulate form of beta-(1--> 3)-D-glucan from Saccharomyces cerevisiae for its ability to induce proinflammatory cytokine secretion in mouse peritoneal macrophages in vitro, and we have examined the effect of IFN-gamma. MG was rapidly phagocytized by peritoneal macrophages, and these MG-treated macrophages upregulated TNF-alpha, IL-6, and IL-1beta mRNAs and secreted these proinflammatory cytokines. These data suggest that a synergy between IFN-gamma and beta-glucan may have evolved to lower the threshold of sensitivity of the innate immune response to fungal pathogens." [respond faster in attacking fungal pathogens – mycotoxins]*

Nitric Oxide Synthesis:

Ohno N, et al; *"Effect of beta-glucans on the nitric oxide synthesis by peritoneal macrophages in mice;"* Biol. Pharm. Bull. 19:608-612; 1996.

Hunter Jr. KW, Gault R, Jordan F, *"Mode of Action of B-Glucan Immunopotentiators,"* Department of Microbiology, University of Nevada School of Medicine, Oct 1998. **Direct Quote:** *"...these data do indicate Glucan particle size is an important factor in the production of nitric oxide. Nitric oxide is generated during the "oxidative burst" that kills ingested microbes [bacteria, viruses, fungi, parasites, etc]. This would suggest that the small particle glucan has greater ability to enhance the immune system than the globular form of glucan."*

Organ Injury - Sepsis:

Sener G, Toklu H, et al; *"Protective effect of beta-glucan against oxidative organ injury in a rat model of sepsis,"* Int Immunopharmacol:1387-96 Epub 2005/Aug 2005. **Direct Quote:** *"Sepsis leads to various organ damage and dysfunction. One of the underlying mechanisms is thought to be oxidative damage due to generation of free radicals. ...Elevated plasma TNF-alpha levels in septic rats [was] significantly reduced to control levels in beta-glucan treated rats. Since beta-glucan administration reversed these oxidant responses, it seems likely that beta-glucan protects against sepsis-induced oxidative organ injury."*

Oxidative Damage/Stress:

Sener G, Eksioglu-Demiraop E, Cetiner M, Ercan F, Yegen BC; *"beta-glucan ameliorates methotrexate-induced oxidative organ injury via its antioxidant and immunomodulatory effects."* European J Pharmacology; 542(1-3):170-178; Epub May 2006. Aug 7 2006. **Direct Quote:** *"Methotrexate is an antifolate [antimetabolite chemotherapy drug] that is widely used in the treatment of rheumatic disorders and malignant tumors. The efficacy of methotrexate is often limited by severe side effects and toxic sequelae [disease condition caused by a disease], where oxidative stress [free radical damage] is noticeable. ... Thus, the findings of the present study suggest that beta-glucan, through its antioxidant and immunoregulatory effects, may be of therapeutic value in alleviating the leukocyte apoptosis [white immune cell death], oxidative [free radical] tissue injury and thereby the intestinal and hepatorenal [liver or kidney] side effects of methotrexate treatment."*

Oxidative Damage:

Toklu HZ, Sehirili AO, Velioglu-Ogunc A, Centinel S, Sener G; *"Acetaminophen-induced toxicity is*

prevented by beta-d-glucan treatment in mice." European J Pharmacology; 543(1-3):133-40; Epub 2006 Jun; Jun 2, 2006. **Direct Quote:** *"The protective effect of beta-glucan against oxidative injury caused by acetaminophen [Tylenol, Anacin 3, Tempra, Datriil] was studied in mice liver...Acetaminophen caused a significant decrease in the GSH level of the tissue, which was accompanied with significant increases in the hepatic luminol and lucigenin chemiluminescence values, malondialdehyde level, MPO activity and collagen content. Similarly, serum ALT, AST levels, as well as LDH and TNF-alpha, were elevated in the acetaminophen-treated group...beta-d-glucan treatment reversed all of these [liver toxicity] biochemical indices, as well as histopathological alterations that were induced by acetaminophen. In conclusion, these results suggest that beta-d-glucan exerts cytoprotective effects against oxidative injury through its antioxidant properties and may be of therapeutic use in preventing acetaminophen toxicity."*

Toklu HZ, Sener G, "Beta-glucan protects against burn-induced oxidative organ damage in rats," Int. Immunopharmacol; 6(2):156-69, Marmara U., Istanbul, Turkey; Epub Aug 2005/Feb 2006. **Direct Quote:** *"Thermal injury may lead to systemic inflammatory response, and multiple organ failure. The results indicate that both systemic and local administration of beta-glucan were effective against burn-induced oxidative tissue damage in the rat. Beta-glucan, besides their immunomodulatory effects, have additional antioxidant properties. Therefore, beta-glucans merit consideration as therapeutic agents in the treatment of burn injuries."*

Sener G, Eksioglu-Demiraop E, Cetiner M, Ercan F, Yegen BC; "beta-glucan ameliorates methotrexate-induced oxidative organ injury via its antioxidant and immunomodulatory effects." European J Pharmacology; 542(1-3):170-178; Epub May 2006. Aug 7 2006. **Direct Quote:** *"Methotrexate is an antifolate that is widely used in the treatment of rheumatic disorders and malignant tumors. The efficacy of methotrexate is often limited by severe side effects and toxic sequelae [disease condition caused by a disease], where oxidative stress is noticeable. ... Thus, the findings of the present study suggest that beta-glucan, through its antioxidant and immunoregulatory effects, may be of therapeutic value in alleviating the leukocyte apoptosis [white immune cell death], oxidative tissue injury and thereby the intestinal and hepatorenal [liver or kidney] side effects of methotrexate treatment."*

Parasites:

Williams D.L., Browder I. and DiLuzio N.R., "Soluble phosphorylated glucan: methods and compositions for wound healing," U.S. Patent 4975421, Issued Dec 4, 1990. **Direct Quote:** *"The soluble phosphorylated glucans are useful for promoting the wound healing process. The soluble phosphorylated glucans are also useful for prophylactic and therapeutic applications against neoplastic, bacteria, viral, fungal and parasitic diseases."*

DiLuzio N.R., "Immunopharmacology of glucan: a broad spectrum enhancer of host defense mechanisms," Trends in Pharmacol. SCI., 4:344-347. Dept of Physiology, Tulane U, New Orleans, LA. 1983. **Direct Quote:** (p347) *"The broad spectrum of immunopharmacological activities of glucan includes not only the modification of certain bacterial, fungal, viral and parasitic infections, but also inhibition of tumor growth."*

DiLuzio N.R. and Williams D.L., "The Roll of Glucan in the Prevention and Modification of Microparasitic Diseases;" in Chemical Regulation of Immunology in Veterinary Medicine, Alan R. Liss, Inc.; pp. 443-456. 1984.

Particle Size:

Hunter KW, Gault RA, Berner MD, "Preparation of microparticulate B-glucan from *Saccharomyces cerevisiae* for use in immune potentiation." Letters in Applied Microbiology, Vol 35 Issue 4, 267-271, October 2002 **Direct Quote:** "...there was evidence that macrophages, key target cells for the immunopharmacological activity of B-glucans, preferentially ingest particles in the 1-2- μ (micron) diameter size range. Compared with the aggregated [5-100- μ micron diameter] form of B-glucan, the B-glucan microparticles remain in suspension longer for pharmaceutical applications and are more effective at enhancing phagocytosis by peritoneal macrophages following oral administration. Although both aggregated and microparticulate glucans enhanced peritoneal macrophage activation when administered orally in mice, the microparticulate glucan was significantly better than the aggregated form"

Jordan F, Hunter Jr. KW, Gault R, "Method for preparing small particle size glucan in a dry material," U.S. Patent 6,476,003. November 2002. **Direct Quote:** "The greater generation and/or production of NO (Nitric Oxide) demonstrates the enhanced activity of the macrophage with a small particle size glucan which is indicative of an activity level of an immune system. ... The measurement of NO production is indicative of an oxidative burst that kills and/or destroys the ingested microbes and/or particles by the macrophage. As a glucan re-aggregates into particles of greater than one micron in diameter, it appears to pass through an animal or human digestive system without substantially complete absorption. ... As the glucan re-aggregates to a size of greater than one micron in diameter, some of the beneficial effect of the glucan is not achieved because the macrophage receptors are not activated as readily by glucan greater than one micron in diameter because the receptor size on corresponding cells and molecules that accept the glucan is generally about one micron in size. ...The greater percentage phagocytosis demonstrates the enhanced activity of the macrophage and the small particle size glucan's ability to activate the immune system."

Hunter Jr. KW, Gault R, Jordan F, "Mode of Action of B-Glucan Immunopotentiators," Department of Microbiology, University of Nevada School of Medicine, Oct 1998.

	Globular Glucan ($\mu\text{g/ml}$)	Sonicated Microparticulate Glucan ($\mu\text{g/ml}$)	Media
Nitric Oxide (μM)	275	600	0

Direct Quote: "...this data does indicate Glucan particle size is an important factor in the production of nitric oxide. Nitric oxide is generated during the "oxidative burst" that kills ingested microbes [bacteria, viruses, fungi, parasites, etc]. This would suggest that the small particle glucan has greater ability to enhance the immune system than the globular form of glucan."

Donzis B. A.; Substantially purified beta (1,3) finely ground yeast cell wall glucan composition with dermatological and nutritional uses; U.S. Patent 5702719; 1997. **Direct Quote:** "The preferred particle size of the fine grind glucan product is about 1.0 micron or less and more preferably, .20 microns or less."

Donzis B. A.; Substantially purified beta (1,3) finely ground yeast cell wall glucan composition with dermatological and nutritional uses; U.S. Patent 5576015; 1996. **Direct Quote:** "Upon oral administration, the smaller or finer particle sized glucan is more quickly dissolved in the gastrointestinal tract and

consequently, more readily absorbed.”

Peritonitis:

Lahnborg G., Hedstrom K.G., Nord C.E.; “*The Effect of Glucan - A Host Resistance Activator and Ampicillin on Experimental Intraabdominal Sepsis*”. Journal of Reticuloendothelial Society. 32: 347-353. 1982 **Direct Quote:** “*It is concluded that glucan, in combination with ampicillin, has a significant effect on the survival rate of rats with induced peritonitis, probably by enhancing the activities of the reticuloendothelial system, an important part of the total host resistance.*”

Platelet Recovery:

Pachen ML, MacVittie TJ, “*Comparative effects of soluble and particulate glucans on survival in irradiated mice*,” J Biol Response Mod 5(1):45-60. Experimental Hematology Dept, Armed Forces Radiobiology Research Inst, Bethesda, MD. Feb 1986. **Direct Quote:** “*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.*”

Pneumonia:

Maurici da Rocha e Silva et al; “*Infection Prevention in Patients with Severe Multiple Trauma with the Immunomodulator Beta 1-3 Polyglucose (glucan)*,” Surgery, Gynecology & Obstetrics; 177:383-388. 1993. **Direct Quote:** “*The incidence of hospital pneumonia of 55% and sepsis of 35% confirms results of previous studies of patients with multitrauma. Glucan decreased pneumonia and sepsis to a significantly lower level of 9.5%....The mortality rate related to infection decreased from 30.0 to 4.8%. The lower number of instances of pneumonia and sepsis....decreased the period of time in the intensive care and the hospital, with a global reduction of 40% on hospital cost.*”

Steele C, Marrero L, Swain S, Harmsen AG, Zheng M, Brown GD, Gordon S, Shellito JE, Kolls JK., “*Alveolar macrophage-mediated killing of Pneumocystis carinii f. sp. muris involves molecular recognition by the Dectin-1 beta-glucan receptor.*” Department of Pediatrics, Division of Pulmonology, Children's Hospital of Pittsburgh, University of Pittsburgh School of Medicine, Pittsburgh, PA 15213, USA. J Exp Med. 198(11): 1677-88; Dec 2003.: **Direct Quote:** “*...these results show that nonopsonic phagocytosis and subsequent killing of P. carinii [a frequent cause of pneumonia in immunocompromised individuals] by alveolar macrophages is dependent upon recognition by the Dectin-1 beta-glucan receptor [activated by beta-glucan ingestion in the Dectin-1 beta-glucan receptor].*”

Maurici da Rocha e Silva et al; “*Infection Prevention in Patients with Severe Multiple Trauma with the Immunomodulator Beta 1-3 Polyglucose (glucan)*,” Surgery, Gynecology & Obstetrics; 177:383-388. 1993. **Direct Quote:** “*The incidence of hospital pneumonia of 55% and sepsis of 35% confirms results of previous studies of patients with multitrauma. Glucan decreased pneumonia and sepsis to a significantly lower level of 9.5%....The mortality rate related to infection decreased from 30.0 to 4.8%. The lower number of instances of pneumonia and sepsis....decreased the period of time in the intensive care and the hospital, with a global reduction of 40% on hospital cost.*”

Protozoan Infections:

Jamas S, Easson D, Ostroff G: "Underivatized aqueous soluble beta (1,3) glucan, composition and method of making same." U.S. Patent Application 20020032170, March 14, 2002. **Direct Quote:** "The use of soluble and insoluble beta glucans alone or as vaccine adjuvants for viral and bacterial antigens has been shown in animal models to markedly increase resistance to a variety of bacterial, fungal, protozoan and viral infections."

Radiation (Irradiation):

Daniel E Cramer, Daniel J Allendorf, Jarek T Baran, Richard Hansen, Jose Marroquin, Bing Li, Janina Ratajczak, Mariusz Z Ratajczak, and Jun Yan: "Beta-glucan enhances complement-mediated hematopoietic recovery after bone marrow injury;" Blood; DOI 10.1182. Tumor Immunobiology Program and Stem Cell Biology Program, James Graham Brown Cancer Center, University of Louisville, Louisville, KY, USA. Sept 2005. **Direct Quote:** "...Myelotoxic injury in the bone marrow (BM) as a consequence of total body irradiation (TBI) or granulocyte colony stimulating factor (G-CSF) mobilization results in the deposition of iC3b on BM [bone marrow] stroma [cell framework]. ... Taken together, these observations suggest a novel role for C, CR3, and Beta glucan in the restoration of hematopoiesis [cell formation] following injury." NOTE: Mice were treated for 12 days with beta glucan and exposed to a sublethal dose of radiation. The beta glucan treated animals had approximately 40 percent more cell formation units in the spleen than untreated mice. When beta glucan was given orally, survival of animals receiving a lethal dose of radiation after stem cell transplantation was significantly enhanced. Forty days following radiation exposure, approximately 30 percent of mice treated with beta glucan survived compared with only 3 percent of untreated animals.

Gu YH, Takagi Y, et al; "Enhancement of radioprotection and anti-tumor immunity by yeast-derived beta-glucan in mice," J Med Food. 8(2) 154-8; Dept of Radiological Technology, Suzuka U of Med Sc, Suzuka, Japan, Summer 2005. **Direct Quote:** "Intraperitoneal injection of beta-glucan was shown to greatly delay mortality in mice exposed to whole-body X-ray radiation and tumor growth in tumor-bearing mice. ...Augmented immunological activity as seen in increased NK (natural killer) and LAK (lymphokine-activated killer) activity by beta-glucan seems to play a role in preventing secondary infections associated with irradiation and probably contributes to the attenuated [reduced] tumor growth in tumor-bearing mice through enhanced anti-tumour immunity. These results suggest that beta-glucan may be a promising adjunct treatment for cancer patients receiving radiotherapy."

Allendorf D.J., Knudsen G., Elliott T., et al, "Oral Whole Glucan Particles Beta Glucan Treatment Accelerates Myeloid Recovery and Survival after Radiation Exposure." Center for Mind-Body Medicine Comprehensive Care Symposium, April 2003. **Direct Quote:** "Oral treatment with whole glucan particles may be a useful therapeutic intervention following radiation exposure to accelerate myeloid [bone marrow] recovery and increase survival after radiation exposure."

Patchen M.L., Vaudrain T, Correira H, Martin T, Reese D, "In vitro and in vivo hematopoietic activities of Betafectin PGG-glucan.," Exp Hematol, 26(13):1247-54. Dec 1998.

Patchen M.L.; Mork AC, Helmke RJ, Martinez JR, Michalek MT, Zhang GH, "Effects of particulate and soluble(1,3)-beta glucans on Ca²⁺ influx in NR8383 alveolar macrophages," Immunopharmacology, 40(1):77-89. Dept of Pediatrics, U of Texas Health Science Center at San Antonio, Jul 1998. **Direct Quote:** "Benefectin PGG-Glucan, a beta-(1,6) branched beta-(1,3) glucan purified from the cell walls of *Saccharomyces cerevisiae*, has been shown to synergize the myeloid growth factors in vitro and to enhance hematopoietic recovery in myelosuppressed mice and primates. "

Patchen M.L. [V Chrm, Dept of Surg, U of Washington], et al, "Mast Cell Growth Factor(c-kit Ligand) in

Combination with Granulocyte-Macrophage Colony-Stimulating Factor and Interleukin-3: *in vivo* Hemopoietic effects in Irradiated Mice compared to *in vivo* effects”, *Biotherapy*; vol. 7. pp. 13-26. 1994. **Direct Quote:** **“Likewise, although both glucan and granulocyte colony-stimulating factor (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 the G-CSF to further accelerate hemopoietic [formation of blood cells] regeneration and increase survival following radiation-induced myelosuppression [bone marrow suppression].”**

Patchen M.L., D’Alessandro M.M., Brook I., Blakely W.F. McVittie T.J.; “*Glucan: Mechanisms Involved in Its ‘Radioprotective’ Effect*”. *J Leuc Biol.*; 42:95-105. 1987. **Direct Quote:** **“These results suggest that early after irradiation glucan may mediate [convey] its radioprotection by enhancing resistance to microbial invasion via mechanisms not necessarily predicated on hemopoietic [formation of blood cells] recovery. ...glucan can also function as an effective free radical scavenger. Because macrophages have been shown to selectively phagocytize [ingest] and sequester [store] glucan, the possibility that these specific cells may be protected by virtue of glucan’s scavenging ability is also suggested.”**

Pachen ML, MacVittie TJ, “*Comparative effects of soluble and particulate glucans on survival in irradiated mice,*” *J Biol Response Mod* 5(1):45-60. Experimental Hematology Dept, Armed Forces Radiobiology Research Inst, Bethesda, MD. Feb 1986. **Direct Quote:** **“Both glucan-P and glucan-F enhanced the recovery of peripheral blood white cell numbers, platelet numbers, and hematocrit [% of volume of packed red blood cells in a blood sample] values. In addition, both agents increased endogenous pluripotent hemopoietic stem cell numbers in sublethally irradiated mice.”**

Radiation: Patchen M.L., MacVittie T.J., “*Dose-dependent responses of murine pluripotent stem cells and myeloid and erythroid progenitor cells following administration of immunomodulating agent glucan.*” *Immunopharmacology*, 5(4):303-13, Apr 1983. **Direct Quote:** **“The hemopoietic effects produced by six different doses of a commercially available glucan preparation were investigated....bone marrow pluripotent stem cells (CFU-s) content increased...In the spleen, all aspects of hemopoiesis [formation of blood cells] increased after glucan administration.”**

Patchen M.L., McVittie T.J.; *Temporal Response of Murine Pluripotent Stem Cells and Myeloid and Erythroid Progenitor Cells to Low-dose Glucan Treatment.* *Acta Hemat*; 70:281-288. Experimental Hematology Dept, Armed Forces Radiobiology Research Inst, Bethesda, MD. 1983. **Direct Quote:** **“Clearly, there are numerous possible uses for an agent such as glucan, which is a potent stimulator of hemopoietic activity. Currently, we [U.S. Armed Services] are using glucan to enhance hemopoietic proliferation in conjunction with hemopoietic injury induced by radiation.”**

White Blood Cell – Recovery:

Pachen ML, MacVittie TJ, “*Comparative effects of soluble and particulate glucans on survival in irradiated mice,*” *J Biol Response Mod* 5(1):45-60. Experimental Hematology Dept, Armed Forces Radiobiology Research Inst, Bethesda, MD. Feb 1986. **Direct Quote:** **“Both glucan-P[articulate] 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.”**

Carrow, D.J. M.D.; “*Beta-1,3-glucan as a Primary Immune Activator,*” *Townsend Letter*; June 1996. **Direct Quote:** **“The following list includes benefits from the use of Beta 1,3-glucan supplementation: People who have impaired immunity from any cause ...; have a high occurrence of infectious**

diseases; have tumors and/or those undergoing chemotherapy or radiation therapy; are over forty who are concerned about the natural aging process or might have noticed a slowing down of immune reactivity; who are geriatric patients; and other with compromised immune disorders."

Rheumatoid Arthritis:

Sener G, Eksioglu-Demiraop E, Cetiner M, Ercan F, Yegen BC; "beta-glucan ameliorates methotrexate-induced oxidative organ injury via its antioxidant and immunomodulatory effects." European J Pharmacology; 542(1-3):170-178; Epub May 2006. Aug 7 2006. **Direct Quote:** "*Methotrexate is an antifolate that is widely used in the treatment of rheumatic disorders and malignant tumors. The efficacy of methotrexate is often limited by severe side effects and toxic sequelae [disease condition caused by a disease], where oxidative stress is noticeable. ... Thus, the findings of the present study suggest that beta-glucan, through its antioxidant and immunoregulatory effects, may be of therapeutic value in alleviating the leukocyte apoptosis [white immune cell death], oxidative tissue injury and thereby the intestinal and hepatorenal [liver or kidney] side effects of methotrexate treatment."*

Safety – FDA Classification:

Carrow, D.J. MD; "Beta-1,3-glucan as a Primary Immune Activator," Townsend Letter; June 1996. **Direct Quote:** "*Beta 1,3-glucan is a safe and potent nutritional supplement with a profound systemic effect that can be described as nonspecific immune stimulation combined with its free radical scavenging activity. Remember, beta 1,3-glucan is generally recognized as safe (category GRAS, according to FDA) and has no known toxicity or side effects."*

Federal Drug Administration, "Appendix A Food Additives," Yeast extract (Bakers) – FL/ADJ, GRAS, See Specs 184.1983. Washington DC. <http://www.fda.gov> 1997.

Williams D.L., et al; "Pre-clinical Safety Evaluation of Soluble Glucan", Int. J. Immunopharmac. Vol. 10, No. 4: 405-414. Dept of Phys, Tulane U Sch of Med, New Orleans, LA. 1988. **Direct Quote:** "*Soluble glucan, a beta-1,3-linked glucopyranose biological response modifier, is effective in the therapy of experimental neoplasia, infectious diseases and immune suppression."*

Sarcoma:

Seljelid R, et al, "Evidence that tumor necrosis induced by an irradiated beta 1-3D polyglucose is mediated by a concerted action of local and systemic cytokines," Scand J Immuno 30(6): 687-694. Dec 1989. **Direct Quote:** "*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 [in the body] and in macrophage cultures in vitro [out of body]."*

Williams DL, et al, "Therapeutic efficacy of glucan in a murine model of hepatic metastatic disease," Hepatology 5(2):198-206. Mar 1985. **Direct Quote:** "*...coincubation of particulate glucan with diverse*

populations of normal or tumor cells in vitro indicated that glucan exerted a direct cytostatic effect on sarcoma and melanoma cells and, in contrast, had a proliferative effect on normal spleen and bone marrow cells."

Sepsis-Intra-abdominal:

Tzianabos AO, Cisnerol RL, et al; "Protection against intra-abdominal sepsis by two polysaccharide immunomodulators (Beta 1,3/1,6 glucan)," J Infect Dis, 178:1,200-6. 1998. **Direct Quote:** "These data demonstrate the usefulness of [Beta 1,3/1,6 glucan]... in preventing experimental intraabdominal sepsis...and may represent a new adjunct to antibiotic regimens currently used to prevent clinical cases of this disease"

Sepsis:

Sener G, Toklu H, et al; "Protective effect of beta-glucan against oxidative organ injury in a rat model of sepsis," Int Immunopharmacol:1387-96 Epub 2005/Aug 2005. **Direct Quote:** "Sepsis leads to various organ damage and dysfunction. One of the underlying mechanisms is thought to be oxidative damage due to generation of free radicals. ...Elevated plasma TNF-alpha levels in septic rats [was] significantly reduced to control levels in beta-glucan treated rats. Since beta-glucan administration reversed these oxidant responses, it seems likely that beta-glucan protects against sepsis-induced oxidative organ injury."

Babayigit H, Kucuk C, Sozuer E, Yazici C, Kose K, Akgun H.; "Protective effect of beta-glucan on lung injury after cecal ligation and puncture in rats." Department of General Surgery, School of Medicine, Erciyes University, 38039, Kayseri, Turkey; Intensive Care Med. (6):865-70; Jun 31, 2005.

Direct Quote: "In this rat model of intra-abdominal sepsis beta-glucan treatment partially protected against secondary lung injury, decreased lung hemorrhages, and lung neutrophilia. These results suggest that beta-glucan protects against sepsis-associated lung damage."

Serum Glucose Control:

Pola P, "Composition for the prevention and/or treatment of lipid metabolism disorders and allergic forms," U.S. Patent Application 20030017999, January 23, 2003. **Direct Quote:** ".beta-1,3-D-glucan has proved effective not only in preventing lipid metabolism disorders, but also in stimulating immune defenses, in preventing onset of tumors and in controlling serum glucose."

Skin Regeneration:

Vacher, A M; "Cosmetic composition which includes at least one polysaccharide derived from bacteria of hydrothermal origin," U.S. Patent Application 20020187167, December 12, 2002. **Direct Quote:** "It was shown, for example, that a .beta-glucan which was extracted from the wall of a yeast, i.e. *Saccharomyces cerevisiae*, enabled skin to regenerate."

Ber L., "The Skin Connection;" Natures Impact, Dec 1997. **Direct Quote:** "The effect of a cosmetic regimen containing beta-1,3-glucan on the signs of aging in the skin was evaluated in 150 women, ages 35 to 60. A 27 percent improvement in skin hydration was observed after eight weeks of using the regimen twice a day. A measurable improvement in lines and wrinkles at the end of the study reached 47 percent, firmness and elasticity increased by 60 percent and skin color improved by 26

percent."

Spinal Cord Injury:

Kayali H, Ozdag MF, Kahraman S, Aydin A, Gonul E, Sayal A, Odabasi Z, Timurkaynak E.; "The antioxidant effect of beta-Glucan on oxidative stress status in experimental spinal cord injury in rats." Dept Neurosurgery, Gulhane Military Medical Academy, Ankara, Turkey; Neurosurg Rev. Apr 30 2005; **Direct Quote:** "According to our results, beta-Glucan works like a scavenger and has an antioxidant effect on lipid peroxidation [free radical damage] in spinal cord injury."

Staphylococcus, Candida albicans and Infectious Challenge:

Rice PJ, Adams EL, Ozment-Skelton T, Gonzales A, Goldman MP, Lockhart BE, Barker LA, Breuel KF, Deponti WK, Kalbfleisch JH, Ensley HE, Brown GD, Gordon S, Williams DL.; "Oral delivery and gastrointestinal absorption of soluble glucans stimulate increased resistance to infectious challenge." East Tennessee State University. J Pharmacol Exp Ther. Jun 23, 2005. **Direct Quote:** "Oral glucan administration also increased survival in mice challenged with *Staphylococcus aureus* or *Candida albicans* ...[and] increase[s] IL-12 expression and induce[s] protection against infectious challenge."

Kokoshis PL, DiLuzio NR et al, "Increased resistance to *Staphylococcus aureus* infection and enhancement in serum lysozyme activity by glucan." Science, 199(4335);1340-1342; 1978: **Direct Quote:** "Prior treatment of mice with glucan significantly enhanced their survival when they were challenged systemically with *Staphylococcus aureus*. These studies indicate glucan confers an enhanced state of host defense against bacterial infections."

Onderdonk, A.B., et al., "Anti-Infective Effect of Poly-.beta.1-6 -Glucotriosyl-.beta.1-3-Glucopyranose Glucan In Vivo," Infec. Immun.; 60:1642-1647. 1992. Dept of Pathology, Channing Lab, Brigham and Women's Hospital, Boston, MA. **Direct Quote:** "Mice challenged with *Escherichia coli* or *Staphylococcus aureus* were protected against lethal peritonitis by the intravenous administration of 10 micrograms of poly-beta 1-6-glucotriosyl-beta 1-3-glucopyranose (PGG) glucan per animal 4 to 6 h prior to bacterial challenge."

Stem Cell Transplantation:

Daniel E Cramer, Daniel J Allendorf, Jarek T Baran, Richard Hansen, Jose Marroquin, Bing Li, Janina Ratajczak, Mariusz Z Ratajczak, and Jun Yan; "Beta-glucan enhances complement-mediated hematopoietic recovery after bone marrow injury;" Blood; DOI 10.1182. Tumor Immunobiology Program and Stem Cell Biology Program, James Graham Brown Cancer Center, University of Louisville, Louisville, KY, USA. Sept 2005. **Direct Quote:** "...Myelotoxic injury in the bone marrow (BM) as a consequence of total body irradiation (TBI) or granulocyte colony stimulating factor (G-CSF) mobilization results in the deposition of iC3b on BM [bone marrow] stroma [cell framework]. ... Taken together, these observations suggest a novel role for C, CR3, and Beta glucan in the restoration of hematopoiesis [cell formation] following injury." NOTE: Mice were treated for 12 days with beta glucan and exposed to a sublethal dose of radiation. The beta glucan treated animals had approximately 40 percent more cell formation units in the spleen than untreated mice. When beta glucan was given orally, survival of animals receiving a lethal dose of radiation after stem cell transplantation was significantly enhanced. Forty days following radiation exposure, approximately 30 percent of mice treated with beta glucan survived compared with only 3 percent of the untreated animals.

Stress – Physical or Emotional:

Carrow, D.J.; "Beta-1,3-glucan as a Primary Immune Activator," Townsend Letter; June 1996. **Direct Quote:** *"The following list includes benefits from the use of Beta 1,3-glucan supplementation: Professional and amateur athletes as well as people who work outdoors intensively. People under physical or emotional stress"*

Structure – Beta Glucan and Immune System:

Czop J.K., Gurish M.F., Kadish J.L., *Production and Isolation of Rabbit Anti-idiotypic Antibodies Directed Against the Human Monocyte Receptor for Yeast B-glucans.* Journal of Immunology; 145:995-1001. Dept of Med, Harvard Med Sch, Boston, MA. 1990. **Direct Quote (p1):** *"Beta-Glucans with 1,3 and/or 1,6 linkages are the major structural components of yeasts and fungi and are pharmacologic agents in animals...The cell wall glucans of S. cerevisiae consist of two structurally distinct Beta-glucans: major components comprised of consecutively, 1,3-linked glucopyranosyl residues with small numbers of 1,6-linked branches, and minor components with consecutive 1,6-linkages and 1,3-branches."*

Thermal Injury:

Toklu HZ, Sener G, *"Beta-glucan protects against burn-induced oxidative organ damage in rats,"* Int. Immunopharmacol; 6(2):156-69, Marmara U., Istanbul, Turkey; Epub Aug 2005/Feb 2006. **Direct Quote:** *"Thermal injury may lead to systemic inflammatory response, and multiple organ failure. The results indicate that both systemic and local administration of beta-glucan were effective against burn-induced oxidative tissue damage in the rat. Beta-glucan, besides their immunomodulatory effects, have additional antioxidant properties. Therefore, beta-glucans merit consideration as therapeutic agents in the treatment of burn injuries."*

Tissue Damage:

Oxidative Burn Injuries: Toklu HZ, Sener G, *"Beta-glucan protects against burn-induced oxidative organ damage in rats,"* Int. Immunopharmacol; 6(2):156-69, Marmara U., Istanbul, Turkey; Epub Aug 2005/Feb 2006. **Direct Quote:** *"The results indicate that both systemic and local administration of beta-glucan were effective against burn-induced oxidative tissue damage in the rat. Beta-glucan, besides their immunomodulatory effects, have additional antioxidant properties. Therefore, beta-glucans merit consideration as therapeutic agents in the treatment of burn injuries."*

Transplantation - Stem Cells:

Daniel E Cramer, Daniel J Allendorf, Jarek T Baran, Richard Hansen, Jose Marroquin, Bing Li, Janina Ratajczak, Mariusz Z Ratajczak, and Jun Yan; *"Beta-glucan enhances complement-mediated hematopoietic recovery after bone marrow injury,"* Blood; DOI 10.1182. Tumor Immunobiology Program and Stem Cell Biology Program, James Graham Brown Cancer Center, University of Louisville, Louisville, KY, USA. Sept 2005. **Direct Quote:** *"...Myelotoxic injury in the bone marrow (BM) as a consequence of total body irradiation (TBI) or granulocyte colony stimulating factor (G-CSF) mobilization results in the deposition of iC3b on BM [bone marrow] stroma [cell framework]. ... Taken together, these observations suggest a novel role for C, CR3, and Beta glucan in the restoration of hematopoiesis [cell formation] following [bone marrow] injury."* NOTE: Mice were treated for 12 days with beta glucan and exposed to a sublethal dose of radiation. The beta glucan treated animals had

approximately 40 percent more cell formation units in the spleen than untreated mice. When beta glucan was given orally, survival of animals receiving a lethal dose of radiation after stem cell transplantation was significantly enhanced. Forty days following radiation exposure, approximately 30 percent of mice treated with beta glucan survived compared with only 3 percent of untreated animals. Researchers discovered beta-glucan enhances the proliferation of stem cells, promoting white blood cell recovery in bone marrow injury and repair.

Trauma:

Jamas S, Easson D, Ostroff G: "Underivatized aqueous soluble beta (1,3) glucan, composition and method of making same." U.S. Patent Application 20020032170, March 14, 2002. **Direct Quote:** "**Beta-glucan was shown to be beneficial in animal models of trauma, wound healing and tumorigenesis.**"

Browder IW., Williams D., Pretus H., et al; *Beneficial Effect of Enhanced Macrophage Function in the Trauma Patients.* Ann. Surg.; Vol 211: 605-613. Dept of Surg and Physiol, Tulane U Sch of Med, LA and Istituto Di Chirurgia D'Urgenza, U of Torino, Torino, Italy. 1990. **Direct Quote:** "**Previous studies have demonstrated that glucan, a beta-1,3-linked glucopyranose polymer, isolated from the inner cell wall of Saccharomyces cerevisiae, is a potent macrophage stimulant and is beneficial in the therapy of experimental bacterial, viral, and fungal diseases. Use of glucan in a murine model of hind-limb crush injury decreased macrophage PGE2 release while stimulating bone marrow proliferation.**"

Maurici da Rocha e Silva et al; "Infection Prevention in Patients with Severe Multiple Trauma with the Immunomodulator Beta 1-3 Polyglucose (glucan);" Surgery, Gynecology & Obstetrics; 177:383-388. 1993. **Direct Quote:** "**The incidence of hospital pneumonia of 55% and sepsis of 35% confirms results of previous studies of patients with multitrauma. Glucan decreased pneumonia and sepsis to a significantly lower level of 9.5%....The mortality rate related to infection decreased from 30.0 to 4.8%. The lower number of instances of pneumonia and sepsis....decreased the period of time in the intensive care and the hospital, with a global reduction of 40% on hospital cost.**"

Tuberculosis:

Hetland G, Sandven P; "Beta-1,3-Glucan reduces growth of Mycobacterium tuberculosis in macrophage cultures," FEMS Immunol Med Microbiol 25;33(1):41-5. Mar 2002. **Direct Quote:** "**The results indicate that beta-glucans inhibit growth of M. tuberculosis in host cells in vitro, probably due to cellular stimulation and/or competitive inhibition of uptake of bacteria via CR3 (CD11b/18).**"

Tumors:

Lamas S, Easson D, Ostroff G: "Underivatized aqueous soluble beta (1,3) glucan, composition and method of making same." U.S. Patent Application 20020032170, March 14, 2002. **Direct Quote:** "**Beta-glucan was shown to be beneficial in animal models of trauma, wound healing and tumorigenesis [formation or production of tumors].**"

Sener G, Eksioglu-Demiraop E, Cetiner M, Ercan F, Yegen BC; "beta-glucan ameliorates methotrexate-induced oxidative organ injury via its antioxidant and immunomodulatory effects." European J Pharmacology; 542(1-3):170-178; Epub May 2006. Aug 7 2006. **Direct Quote:** "**Methotrexate is an antifolate [antimetabolite chemotherapy drug] that is widely used in the treatment of rheumatic disorders and malignant tumors. The efficacy of methotrexate is often limited by severe side effects and toxic sequelae [disease condition caused by a disease], where oxidative stress [free radical damage] is noticeable. ... Thus, the findings of the present study suggest that beta-glucan, through**

its antioxidant and immunoregulatory effects, may be of therapeutic value in alleviating the leukocyte apoptosis [white immune cell death], oxidative [free radical] tissue injury and thereby the intestinal and hepatorenal [liver or kidney] side effects of methotrexate treatment."

Gu YH, Takagi Y, et al; "Enhancement of radioprotection and anti-tumor immunity by yeast-derived beta-glucan in mice," J Med Food. 8(2) 154-8; Dept of Radiological Technology, Suzuka U of Med Sc, Suzuka, Japan, Summer 2005. **Direct Quote:** *"Intraperitoneal injection of beta-glucan was shown to greatly delay mortality in mice exposed to whole-body X-ray radiation and tumor growth in tumor-bearing mice. ...Augmented immunological activity as seen in increased NK (natural killer) and LAK (lymphokine-activated killer) activity by beta-glucan seems to play a role in preventing secondary infections associated with irradiation and probably contributes to the attenuated [reduced] tumor growth in tumor-bearing mice through enhanced anti-tumour immunity. These results suggest that beta-glucan may be a promising adjunct treatment for cancer patients receiving radiotherapy."*

Li B, Allendorf D, Hansen R, Marroquin J, Ding C, Cramer DE, Yan J; "Yeast beta-Glucan Amplifies Phagocyte Killing of iC3b-Opsonized Tumor Cells via Complement Receptor 3-Syk-Phosphatidylinositol 3-Kinase Pathway." J Immunology: 1:177(3):1661-9. Tumor Immunobiology Program, James Graham Brown Cancer Center, University of Louisville, Louisville, KY. Aug 2006. **Direct Quote:** *Anti-tumor mAbs [monoclonal antibodies] hold promise for cancer therapy, but are relatively inefficient. ...In this study, we report that tumor-bearing mice treated with a combination of beta-glucan and an anti-tumor mAb show almost complete cessation of tumor growth. beta-glucan, an agent without evident toxicity, may be used to amplify tumor cell killing and may open new opportunities in the immunotherapy of cancer.*

Yan J, Allendorf DJ, Brandley B, "Yeast whole glucan particle (WGP) beta-glucan in conjunction with antitumour monoclonal antibodies to treat cancer." Expert Opin Biol Ther; 5(5):691-702; James Graham Brown Cancer Ctr, Louisville, KY, 2005. **Direct Quote:** *"Extensive studies in preclinical animal tumour models have demonstrated the efficacy of combined oral particulate yeast beta-glucan with antitumour mAb [monoclonal antibodies] in terms of tumour regression and long-term survival. It is proposed that the addition of beta-glucan will further improve the clinical therapeutic efficacy of antitumour mAbs in cancer patients."*

Hong F, Yan J, Baran JT, Allendorf DJ, Hansen RD, Ostroff G, Ross G, "Mechanism by Which Orally Administered B-1,3-Glucans Enhance the Tumoricidal Activity of Antitumor Monoclonal Antibodies in Murine Tumor Models," The J of Immunology 173:797-806. James Graham Brown Cancer Ctr, Louisville, KY; July 15, 2004: **Direct Quote:** *"Orally administered B-1,3-glucans were taken up by macrophages that transported them to spleen, lymph nodes, and bone marrow. Within the bone marrow, the macrophages degraded the large B-1,3 glucans into smaller soluble B-1,3-glucan fragments that were taken up by the CR3 [receptors] of marginated granulocytes [white blood cells formed in the bone marrow]. These granulocytes with CR3-bound B-1,3-glucan-fluorescein were shown to kill iC3b-opsonized tumor cells following their recruitment to a site of complement activation resembling a tumor coated with mAb [monoclonal antibodies]."*

Ross G, Hong F, Allendorf D, Hansen R, Ostroff G; "Mechanism of Tumor Regression Stimulated by Yeast Beta Glucan Dietary Supplement." Abstract. April 9, 2003. **Direct Quote:** *"The mechanism of B-glucan enhancement of tumor mAb immunotherapy involves the activation of the innate immune cells (macrophages and neutrophils) via the lectin binding site on CR3 to target and kill Ab opsonized tumor cells. Oral yeast B-glucan is orally absorbed and transported by macrophages into immune tissues and tumors resulting in the secretion of inflammatory cytokines and soluble B-glucan leading to an enhanced innate immune cell attack against tumor cells."*

Pola P, "Composition for the prevention and/or treatment of lipid metabolism disorders and allergic forms," U.S. Patent Application 20030017999, January 23, 2003. **Direct Quote:** ".beta-1,3-D-glucan has proved effective not only in preventing lipid metabolism disorders, but also in stimulating immune defenses, in preventing onset of tumors and in controlling serum glucose."

Cheung NK, Modak S, Vickers A, Knuckles B; "Orally administered beta-glucans enhance anti-tumor effects of monoclonal antibodies," Department of Pediatrics, Memorial Sloan-Kettering Cancer Center, Cancer Immunology, Immunotherapy ;51(10):557-64. Dec 2002. **Direct Quote:** "We studied readily available (1-->3)-beta- D-glucan using the immune deficient xenograft tumor models, and examined the relationship of its anti-tumor effect Given the favorable efficacy and toxicity profile of oral beta-D-glucan treatment, the role of natural products that contain beta-glucan in cancer treatment as an enhancer of the effect of mAb therapy deserves further study."

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DiLuzio N.R., Hoffman E.D., "Glucan-induced enhancement of host resistance to experimental tumors."

Prog. Cancer Therapy, 2: 475-499. 1977.

DiLuzio N.R., Williams D.L., et al, "Comparative tumor-inhibitory and anti-bacterial activity of soluble and particulate glucan," Int J Cancer, 24(6):773-779. Dec 1979 **Direct Quote:** "...these studies demonstrate that a soluble glucan preparation exhibits significant anti-tumor and anti-staphylococcal activity."

DiLuzio N.R., "Immunopharmacology of glucan: a broad spectrum enhancer of host defense mechanisms," Trends in Pharmacol. SCI., 4:344-347. Dept of Physiology, Tulane U, New Orleans, LA. 1983. **Direct Quote:** (p347) "The broad spectrum of immunopharmacological activities of glucan includes not only the modification of certain bacterial, fungal, viral and parasitic infections, but also inhibition of tumor growth."

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. 47:4842-4847. 1987.

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Proctor, et al., "Development of a Bioassay for Anti-Tumor Activity of the Reticuloendothelial Stimulant Class: Reproducibility of the Bioassay". J. Immunopharmacol.; 3: 385-395. 1981-1982 **Direct Quote:** "Intravenously administered DiLuzio glucan...caused dose dependent increases in the tumor cell loss from the lungs of ...mice challenged respectively with intravenous ¹²⁵IuDR labelled B16 or T 1699 mammary carcinoma cells."

Penna C, Dean P, Nelson H (Dept of Surgery-Mayo Clinic); "Pulmonary metastases neutralization and tumor rejection by in vivo administration of beta glucan and bispecific antibody;" Int J Cancer, 65:3,377-82. Jan 1996.

Direct Quote: "In the established tumor model, beta glucan + Bispecific antibody (BsAb) reduced the incidence of s.c. tumors as compared with control...It also prolonged survival of tumor-bearing mice compared with control. We conclude that T cells can be activated in vivo by beta glucan..."

Ulcers – Decubitus:

Browder I.W., DiLuzio N.R., et al. "Enhanced Healing of Decubitus Ulcers by Topical Application of Particulate Glucan." Tulane University School of Medicine; Research Summary. 1984.

Ulcers, Pressure

Sener G, Sert G, Ozer SA, Arbak S, Uslu B, Gedik N, Avanoğlu-Dulger G; "Pressure ulcer-induced oxidative organ injury is ameliorated by beta-glucan treatment in rats." Int Immunopharmacol:6(5):724-32; Marmara U, Sch of Pharmacy, Dept Pharmacology, Div Biochemistry; Epub Nov 2005; May 2006. **Direct Quote:** "Pressure ulcers (PU) cause morphological and functional alterations in the skin and visceral organs. ... Local treatment with beta-glucan inhibited the increase in MDA and MPO levels and the decrease in GSH in the skin induced by (PU), ... systemic treatment prevented the damage in the visceral organs. Significant increases in creatinine, BUN, ALT, AST, LDH and collagen levels in PU [Pressure Ulcers] group were prevented by beta-glucan treatment. ... Tissue injury was

decreased. ... Thus, supplementing geriatric and neurologically impaired patients with adjuvant therapy of beta-glucan may have some benefits for successful therapy and improving quality of life."

Viral Diseases:

Browder IW., Williams D., Pretus H., et al; "Beneficial Effect of Enhanced Macrophage Function in the Trauma Patients." Ann. Surg.; Vol 211: 605-613. Dept of Surg and Physiol, Tulane U Sch of Med, LA and Istituto Di Chirurgia D'Urgenza, U of Torino, Torino, Italy. 1990. **Direct Quote:** "*Previous studies have demonstrated that glucan, a beta-1,3-linked glucopyranose polymer, isolated from the inner cell wall of Saccharomyces cerevisiae, is a potent macrophage stimulant and is beneficial in the therapy of experimental bacterial, viral, and fungal diseases.*"

Jamas S, Easson D, Ostroff G: "Underivatized aqueous soluble beta (1,3) glucan, composition and method of making same." U.S. Patent Application 20020032170, March 14, 2002. **Direct Quote:** "*The use of soluble and insoluble beta glucans alone or as vaccine adjuvants for viral and bacterial antigens has been shown in animal models to markedly increase resistance to a variety of bacterial, fungal, protozoan and viral infections.*"

Czop, Joyce K., "The Role of Beta.-Glucan Receptors on Blood and Tissue Leukocytes in Phagocytosis and Metabolic Activation". Pathology and Immunopathology Research; 5:286-296. Harvard Medical School. 1986. **Direct Quote:** "*...the presence of a particulate activator can rapidly initiate assembly and amplification of a host defense system involving humoral and cellular interactions with B-glucans. ...Animals pretreated with purified glucan particles are subsequently more resistant to bacterial, viral, fungal, and protozoan challenge, reject antigenically incompatible grafts more rapidly and produce higher titers of serum antibodies to specific antigens.*"

DiLuzio N.R., "Immunopharmacology of glucan: a broad spectrum enhancer of host defense mechanisms," Trends in Pharmacol. SCI., 4:344-347. Dept of Physiology, Tulane U, New Orleans, LA. 1983. **Direct Quote:** "*The broad spectrum of immunopharmacological activities of glucan includes not only the modification of certain bacterial, fungal, viral and parasitic infections, but also inhibition of tumor growth.*"

White Blood Cell – Recovery:

Pachen ML, MacVittie TJ, "Comparative effects of soluble and particulate glucans on survival in irradiated mice," J Biol Response Mod 5(1):45-60. Experimental Hematology Dept, Armed Forces Radiobiology Research Inst, Bethesda, MD. Feb 1986. **Direct Quote:** "*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.*"

Wound Healing:

Leibovich S.J., et al., "Promotion of Wound Repair in Mice by Application of Glucan". J. Reticuloendothel. Soc. 27: 1-11. 1980 **Direct Quote:** "*Of all the substances tested, glucan was the only substance to exhibit a particularly marked enhancement of the proliferative phase of wound healing. It appears, from these experiments, that the effect observed by others in terms of the activation of reticuloendothelial [immune response] function by glucan and the activation of macrophages, both locally and systematically, also apply to activation of macrophages in healing wounds.*"

Portera CA, Love EJ, Memore L, Zhang L, Muller A, Browder W, Williams DL; *“Effect of macrophage stimulation on collagen biosynthesis in the healing wound,”* Am Surg, 63:2,125-131. Feb 1997. **Direct Quote:** *“...macrophage modulation with glucan phosphate will increase tensile strength in experimental colon and skin wounds. In addition, we have observed a positive correlation between glucan phosphate treatment, wound tensile strength, and collagen biosynthesis.”*

Williams D.L., Browder I. and DiLuzio N.R., *“Soluble phosphorylated glucan: methods and compositions for wound healing,”* U.S. Patent 4975421, Issued Dec 4, 1990. **Direct Quote:** *“The soluble phosphorylated glucans are useful for promoting the wound healing process. The soluble phosphorylated glucans are also useful for prophylactic and therapeutic applications against neoplastic, bacteria, viral, fungal and parasitic diseases.”*