Research Paper

Effects of Cell Wall Extracts of Gram Positive Bacteria (MPGC) on Human Immunity and Tumor Growth in Animals

Riordan NH, Meng X, Taylor P, Riordan HD. Presented at Comprehensive Cancer Care 2000, Arlington, Virginia, June 2000.

Abstract

Muramyl polysaccharide glycan com plex (MPGC) was tested for its immu nostimulatory effects on human mono nuclear cells and lymphocytes and for its anti-tumor effects in the S-180 mouse sarcoma model. MPGC is a non-toxic purified extract of the bacteri al cell walls of gram-positive bacteria. *In vitro* MPGC (0.1mg/mL stimulated the production of interleukins 1, 6 and 12 and stimulated human lymphocyte proliferation. A mixture of cytokines produced by MPGC (0.1mg/mL) stimu lated human monocytes resulted in the maturation of immature human dendrit ic cells as evidenced by flow cytometric quantification of CD83. Tumors were established in Kun Ming mice (3-4 weeks old, 19-21 grams each, mixed male/female, 10 animals per group) af ter subcutaneous injection of S-180 sarcoma cells in the flank. Intraperito neal MPGC (250 mcg/dose, daily for 14 days, first injection 2 days after tumor establishment) resulted in 75% inhibi tion of tumor growth. Using the same model and conditions, intravenous MPGC (250mcg/dose, daily for 14 days, first injection 2 days after tumor estab lishment) resulted in 77% inhibition of tumor growth compared to controls. We conclude that MPGC has immunos timulatory and anti-tumor qualities and should be studied further as an immuno-therapeutic agent for cancer.

Background

Bacterial and fungal cell wall extracts have been used as immune stimulants and anti-tumor agents. Examples are *Bacillus Calmette-Guerin* (BCG), Poly saccharide K, beta 1,3 glucan, the Mar uyama vaccine and extracts of *Bifido-bacterium, L. lactis, L. fermentum, L acidophilus* and *S. lactis*.

Muramic acid is a component of bacterial cell walls with immunostimulatory quali ties that may be partially responsible for the anti-tumor effects of gram-positive bacterial extracts. Muramyl peptides (comprised of two muramic acids bound together) sensitize macrophages to phos phatidylserine and muramic acid, both of which are found preferentially on tumor cells. Muramyl peptides up-regulate monocyte cytokine genes (IL-1, IL-6, IL-8, IL-12, macrophage chemotactic and activating factor and tumor necrosis fac tor- alpha but not IL-2 or IL10) and acti vate monocyte-mediated tumoricidal ac tivity. Muramyl peptides increase the ability of macrophages to recognize virally infected cells, including cells infected with oncogenic viruses. Muramyl pepti des and muramic acid are not selectively internalized by monocytes and therefore have been associated with toxicity. Mon ocytes/macrophages have mannose re ceptors that allow them to readily inter nalize polysaccharides that contain mannose. Muramyl polysaccharide-glu can complex (MPGC), is a non-toxic bac terial cell wall extract of *Lactobacillus fer mentum* that contains muramic acid moieties attached to variable-length man nose-rich polysaccharides. The man nose-rich polysaccharides promote inter nalization of the entire muramic acid-containing complex.

Animal & Human Studies

S-180 Mouse Tumor Model

Tx (250ug/dose)	Tumor Weight (grams)	Tumor Growth Inhibition
Control	2.40	0%
MPGC IP	0.60	75% p<.001
MPGC IV	0.54	77% p<.001

IP= Intraperitoneal injection IV= Intravenous injection

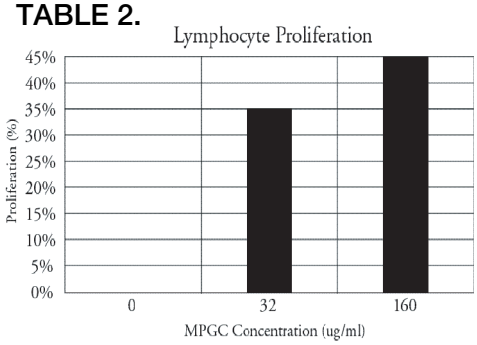
Mouse Sarcoma Model

Table 1 summarizes the inhibitory ef fects of MPGC on sarcoma tumor growth in mice.

Lymphocyte Proliferation

There was a dose dependent increase in lymphocyte proliferation induced by MPGC. The results are summarized in Table 2.

TABLE 2.



Cytokine Production

MPGC significantly induced the produc tion of IL-6 and IL-12 from human monocytes. The results are summar ized in Table 3.

TABLE 3.

FA Extract Effect on MCM Cytokines

FA (mg/ml)	IL-6 (ng/ml)	IL-12 (pg/ml)
0	0	0
0.1	499	1880
1	700	690

Researchers' Conclusion

Research has been presented demon strating that MPGC has immune stimu lating and anti-tumor qualities. MPGC should be studied further to elucidate its anti-tumor effects and mechanisms of actions.

References Available on Request.