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Orally administered particulate beta-glucan modulates tumor-capturing dendritic cells and improves antitumor T-cell responses in cancer

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PMID: 20855461 PMCID: PMC2970627 DOI: 10.1158/1078-0432.CCR-10-0820

Abstract

Purpose: The beneficial properties of β-glucans have been recognized for centuries. Their proposed mechanisms of action in cancer therapy occur via stimulation of macrophages and priming of innate neutrophil complement receptor 3 for eliciting complement receptor 3-dependent cellular cytotoxicity of iC3b-opsonized tumor cells. The current study is to investigate whether β-glucan therapy has any effect on antitumor adaptive T-cell responses.

Experimental design: We first examined the trafficking of orally administered particulate yeast-derived β-glucan and its interaction with dendritic cells (DC) that captured tumor materials. Antigen-specific T cells were adoptively transferred into recipient mice to determine whether oral β-glucan therapy induces augmented T-cell responses. Lewis lung carcinoma and RAM-S lymphoma models were used to test oral β-glucan therapeutic effect. Further mechanistic studies including tumor-infiltrating T cells and cytokine profiles within the tumor milieu were determined.

Results: Orally administered particulate β-glucan trafficked into spleen and lymph nodes and activated DCs that captured dying tumor cells in vivo, leading to the expansion and activation of antigen-specific CD4 and CD8 T cells. In addition, IFN-γ production of tumor-infiltrating T cells and CTL responses were

significantly enhanced on β-glucan treatment, which ultimately resulted in significantly reduced tumor burden. Moreover, β-glucan-treated tumors had significantly more DC infiltration with the activated phenotype and significant levels of Th1-biased cytokines within the tumor microenvironment.

Conclusions: These data highlight the ability of yeast-derived β-glucan to bridge innate and adaptive antitumor immunity and suggest that it can be used as an adjuvant for tumor immunotherapy.

Figures

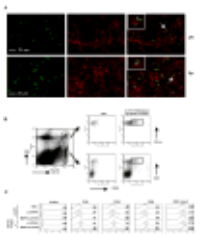

Figure 1. Oral WGPs migrate to the…

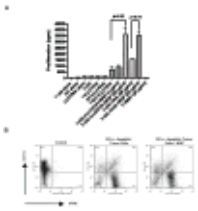

Figure 2. WGPs significantly increase Ag-specific T…

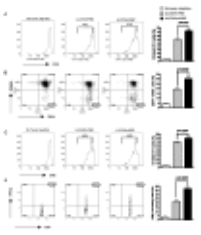

Figure 3. Enhanced Ag-specific T cell responses…

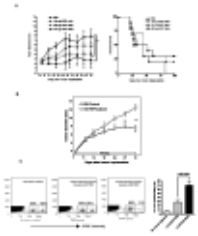

Figure 4. WGP treatment significantly reduces tumor…

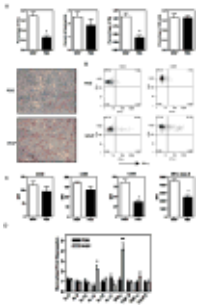

Figure 5. WGP treatment significantly increases IFN-

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