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

PURPOSE: The beneficial properties of beta-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 beta-glucan therapy has any effect on antitumor adaptive T-cell responses.

EXPERIMENTAL DESIGN: We first examined the trafficking of orally administered particulate yeast-derived beta-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 beta-glucan therapy induces augmented T-cell responses. Lewis lung carcinoma and RAM-S lymphoma models were used to test oral beta-glucan therapeutic effect. Further mechanistic studies including tumor-infiltrating T cells and cytokine profiles within the tumor milieu were determined.

RESULTS: Orally administered particulate beta-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 beta-glucan treatment, which ultimately resulted in significantly reduced tumor burden. Moreover, beta-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 beta-glucan to bridge innate and adaptive antitumor immunity and suggest that it can be used as an adjuvant for tumor immunotherapy.