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Orally Administered Particular {beta}-Glucan Modulates Tumor-capturing Dendritic Cells and Improves Anti-tumor T Cell Responses in Cancer.

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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 (CR3) for eliciting CR3-dependent cellular cytotoxicity of iC3b-opsonized tumor cells. The current study is to investigate whether β-glucan therapy has any impact on anti-tumor 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 (DCs) 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 upon 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 anti-tumor immunity and suggest that it can be used as an adjuvant for tumor immunotherapy.

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