Food-derived β-glucans enhance plasticity of M2 macrophages towards new phenotype characterized by production of T cell chemo-attractants

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Introduction: Immune therapies, despite clear clinical effects, are challenged by incomplete and non-durable responses in the majority of tumor-bearing patients. Effective T cell responses are often halted due to the immune suppressive micro-environment, in part related to tumor-associated macrophages. In the current study, we assess non-digestible polysaccharides (ß-glucans) for their 'adjuvant effect' towards innate immune cells to support anti-tumor effects of T cells.
Materials and methods: Nine β-glucans (maitake D-fraction, oat, zymosan, lentinan, curdlan, schizophyllan, whole glucan particles and two types of yeast-derived ß-glucans) were tested for their effects on the plasticity of human monocyte-derived macrophages (M0) that were polarized to immune-suppressive M2 macrophages, often prevalent in solid tumors. Phenotype and function of resulting macrophages were assessed by qPCR, ELISA, flow cytometry, whole genome expression and pathway analysis, flow cytometry and by means of arrays to measure the production of cytokines and chemo-attractants.
Results: Zymosan, yeast and curdlan pushed M2 macrophages towards an M1-like phenotype, in particular showing enhanced expressions of CCR7, ICAM-1 and CD80, and secretion of TNFα and IL-6. Notably, analysis of differentially expressed genes and pathways pointed to enhanced presence of chemo-attractants. Indeed, these β-glucans were shown to induce secretion of chemo-attractants by macrophages in vitro.
Conclusion: These in vitro analyses demonstrate that selected β-glucans have the unique ability to preferentially skew macrophages towards a new phenotype of chemo-attractant-producing macrophages that may sensitize tumors to T cell therapies.

Keywords : Macrophages, tumor microenvironment, repolarization, chemokines
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