Immune complex isolation and characterization is a challenging area of pharmaceutical research. Here, we disclose our efforts to better understand the therapeutically active immune complex formed between Imprime PGG, antibodies, and complement proteins. Imprime PGG is a soluble yeast-derived β-1,3-glucan immunomodulator that is currently being developed as a cancer immunotherapeutic drug. Imprime PGG has shown promising clinical activity in multiple clinical trials in concert with monoclonal antibodies (e.g. bevacizumab and cetuximab). Previous research has demonstrated that Imprime PGG forms an immune complex with anti-β-glucan antibodies, specifically IgG, present in the serum of healthy donors and patients. This immune complex activates the classical complement pathway, leading to opsonization of Imprime PGG by iC3b to form a three-part complex that subsequently binds to the receptors Dectin-1 (beta glucan receptor), CR3 and FcyR on neutrophils and monocytes. The goal of this study is to assemble, isolate, and characterize this complex beginning with the isolation of anti-β-glucan antibodies from serum or commercial sources of immunoglobulin. These antibodies are then combined with pure Imprime PGG and the complexes are characterized. Finally, the biological effect of these Imprime-immune complexes on the activity of myeloid cells (neutrophils, monocytes) will be discussed. In summary, the information learned while isolating and purifying this immune complex will provide a better understanding of Imprime PGG’s mechanism of action.

**Background**

- **Imprime is a pathogen associated molecular pattern (PAMP) molecule under development as an immunotherapy for cancer treatment.**
- **Imprime has been safely administered by iv injection into over 400 human subjects.**
- **It has shown promising efficacy in multiple clinical trials with tumor targeting antibodies including phase 2 clinical trials in lung cancer (NSCLC) and a phase 3 clinical trial in colorectal cancer. Retrospective analyses of these trials have shown an association between anti beta glucan antibody level and clinical outcome.**
- **Imprime also shows synergy with check point inhibitor mAbs in murine in vivo tumor models.**
- **Imprime is isolated from the cell wall of a proprietary strain of Saccharomyces cerevisiae as a pharmaceutical grade, water soluble beta 1,3 linked glucose polymer with beta 1,3 linked side chains of varying length attached in a beta configuration to the 6 position of the main chain glucose residues.**
- **The structure is an aggregate of triple helices with a Mw of ~150 kDa.**

**Objectives**

- To isolate pure endogenous anti beta glucan antibodies (ABA) from pooled human IgG.
- To study the formation of the immune complex between Imprime and ABA by chromatography.
- To assess the biological effects of the purified immune complex on immune function.

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