Imprime PGG modulates the functionality of immunosuppressive myeloid components of the tumor microenvironment and drives enhanced anti-tumor efficacy in combination with anti-PD1 antibody

**Poster #1052**


### Abstract

Checkpoint inhibitor therapies (CPI) have shown great promise, albeit only in a limited percentage of patients. One of the key mechanisms behind the limited efficacy of CPI therapy is immune resistance mediated by immunosuppressive myeloid cells at the tumor microenvironment (TME), namely M2 macrophages and myeloid-derived suppressor cells (MDSCs). Multiple therapeutic interventions are being developed to target these cell types with the intention of reshaping the TME and enhancing the effectors functions of the cytotoxic T cells. Imprime PGG, a novel yeast derived β-glucan PAMP is being clinically developed as an innate immune modulator in combination with anti-PD1 antibody.

In *ex vivo* human and *in vivo* xenograft and syngeneic tumor models, Imprime has been shown to modulate the immunosuppressive tumor-associated macrophages (TAMs) and MDSCs in the spleen as well as TME to an M1 phenotype. The objective of this study was to evaluate Imprime’s ability to modulate the functionality of these suppressive myeloid cells. We chose MC38 colon carcinoma model because it is highly immunogenic and anti-PD-1 antibody alone has significant efficacy which can be further increased by the combination with Imprime. TAMs from Imprime-treated MC38 tumors produced increased levels of TNF-α in response to LPS stimulation. Furthermore, in comparison to the TAMs enriched from tumors treated with anti-PD1 alone, the TAMs enriched from those treated with Imprime and anti-PD1 antibody showed lower expression of indoleamine 2,3-dioxygenase as well as reduced ability to suppress the proliferation of CD3/CD28-stimulated CD3+ splenocytes. Strikingly, the MDSCs enriched from the spleens of Imprime-treated mice also showed decreased suppressive functionality. Along with the antitumor T cell immunity-enhancing changes in myeloid cells, Imprime treatment resulted in increased effector functionality of the tumor-infiltrating CD8 T cells and splenocytes. Collectively, these data show that Imprime is able to remold the immunosuppressive TME to a more functionally active one, thereby enabling the clinical effectiveness of CPI therapy.

### Results

**Imprime synergizes with anti-PD-1 antibody therapy in the murine MC38 tumor model**

![Graph showing Imprime synergizes with anti-PD-1 antibody therapy](image)

**Imprime treatment modulates the functionality of TAMs in the TME**

![Graph showing Imprime treatment modulates TAM functionality](image)

**Systemic Imprime administration alters the immunosuppressive myeloid cells and enhances T cell functionality in the spleen**

![Graph showing Imprime effects on myeloid cells](image)

### Summary

Here we have shown that the systemic treatment of Imprime results in:
- The activation and enhancement of functions of the myeloid cells, including splenic macrophages, MDSCs in spleen and TAMs in tumor.
- The activation and enhancement of the function of CD8 T cells in spleen and tumor.

These findings collectively demonstrate that Imprime is able to repolarize the immunosuppressive TME to a more functionally active one, thereby potentially enhancing the efficacy of CPI therapy.