A novel human TNFR2 antibody (MM-401) modulates T cell responses in anti-cancer immunity

**Introduction**

Despite the dramatic anti-tumor responses observed for immune checkpoint inhibition in subsets of patients, there remains a current need for the larger patient population. Combination immunotherapeutics have been able to improve efficacy, but often at the expense of significant toxicities that are challenging for patients and health care providers. In an effort to improve antibody efficacy, improvements in delivery and the understanding of antibody interaction with the immune system are essential. We have previously demonstrated the ability of MM-401, a human TNFR2 antagonist, to improve T cell function when bound to TNFR2 on T cells.

Materials and methods: Human anti-TNFR2 antibodies were generated in human immunization and after selecting and evaluating human antibodies that were selected by the ability to provide an epitope that was unique to human and both human and mouse TNFR2. Antibody concentrations were generated by transfection of CHO cells with a constructs of an epitope of human TNFR2, and then these were evaluated for binding to CHO cells with a human TNFR2. This antibody was then used to evaluate the ability of the antibody to bind to CHO cells in a panel of CHO cell lines.

Results: Antibody binding to CHO cells was determined by ELISA, and the ability of the antibody to induce anti-TNF activity in the presence of CHO cells in vitro was determined. The results were then compared to a control antibody, and the ability of the antibody to induce anti-TNF activity in vivo was determined.

Conclusions: Our results demonstrate the ability of the antibody to induce anti-TNF activity in vivo, and these studies provide a foundation for further development of the antibody for clinical trials.

**Proliferative Assay**

A proliferative assay was performed to evaluate the ability of the antibody to induce T cell proliferation. The results demonstrated that the antibody significantly increased T cell proliferation, compared to a control antibody. This effect was observed in both human and mouse T cell lines.

**Interleukin-2 (IL-2) Secretion**

IL-2 secretion was measured in the supernatant of T cells stimulated with antibody. The results showed that the antibody significantly increased IL-2 secretion, compared to a control antibody. This effect was observed in both human and mouse T cell lines.

**Antigen-Presenting Cell (APC) Function**

APC function was evaluated by measuring the ability of the antibody to induce costimulation of T cells. The results demonstrated that the antibody significantly increased costimulation, compared to a control antibody. This effect was observed in both human and mouse T cell lines.

**Discussion**

In conclusion, our results demonstrate the ability of the antibody to induce anti-TNF activity in vivo, and these studies provide a foundation for further development of the antibody for clinical trials.

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**References**


**Figure Legends**

**Figure 1**

A: Human TNFR2 antibody binding to CHO cells. The antibody significantly increased binding to CHO cells, compared to a control antibody. This effect was observed in both human and mouse T cell lines.

**Figure 2**

B: Human TNFR2 antibody-induced T cell proliferation. The antibody significantly increased T cell proliferation, compared to a control antibody. This effect was observed in both human and mouse T cell lines.

**Figure 3**

C: Human TNFR2 antibody-induced costimulation. The antibody significantly increased costimulation, compared to a control antibody. This effect was observed in both human and mouse T cell lines.