Enhanced anti-tumor effects by a combination approach of interferon-γ producing recombinant *Bifidobacterium* and anti-mPD-1 antibody in syngeneic mouse model

**Abstract**

Interferon-γ is a cytokine having antitumor activity and has been developed as an anticancer drug in multiple cancer indications. However, we have established human IFN-γ recombinant *Bifidobacterium* specifically inside solid tumor. Both human and murine IFN-γ have growth inhibitory activities against tumor cells and CXCL10 inducing activity for T cells. On the other hand, IFN-γ from IFN-γ secreting E.coli. derived hIFN-γ-DPS showed a modest tumor suppression effect. Induction of PD-L1 by mIFN-γγ induced IFN-γγ from IFN-γγ non-pathogenic anaerobic bacterium modified to secrete IFN-γγ in mice resulted in colonization of IFN-γγ γ in other normal organs. All in together, combination treatment with IFN-γγ and anti-mPD-1 antibody offers a promising tumor therapy.

**Background**

- IFN-γ is a cytokine having antitumor activity and has been developed as an anticancer drug in multiple cancer indications.
- Human and murine IFN-γ have growth inhibitory activities against tumor cells and CXCL10 inducing activity for T cells.
- On the other hand, IFN-γ from IFN-γ secreting E.coli. derived hIFN-γ-DPS showed a modest tumor suppression effect.

**Results**

- Induction of PD-L1 by mIFN-γ induced IFN-γ from IFN-γ non-pathogenic anaerobic bacterium modified to secrete IFN-γ in mice resulted in colonization of IFN-γ in other normal organs.
- In the IFN-γ treated CT26 cells, PD-L1 expression was notably strengthened tumor suppression.

**Conclusion**

- We have established human IFN-γ-DPS and murine IFN-γ-DPS and confirmed secretion of IFN-γ from IFN-γ-DPS and its biological activities.
- Administration of IFN-γ-DPS to CT26 tumor bearing mice resulted in colonization of IFN-γ-DPS and production of IFN-γ only in tumor but not in blood and other normal organs.
- In the IFN-γ treated CT26 cells, PD-L1 expression was enhanced at surface of tumor cells.
- Single treatment of IFN-γ-DPS showed a modest tumor suppression fashion, whereas combination of IFN-γ-DPS and immune checkpoint blocker, anti-mPD-1 antibody notably strengthened tumor suppression.
- All above evidence implied IFN-γ-DPS is a worth-trying combination candidate for anti-PD-1 antibody.

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