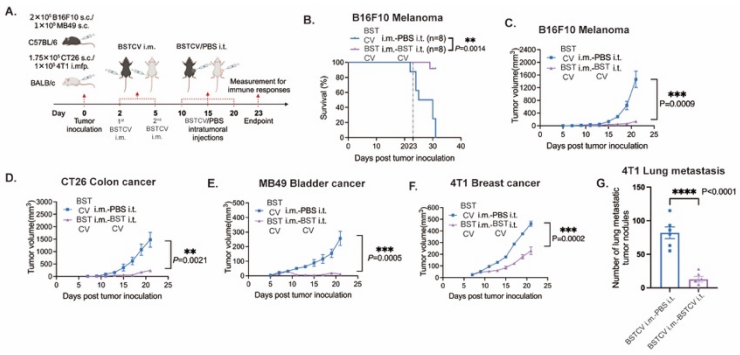
Developing Broad-Spectrum Therapeutic Cancer Vaccines (BSTCV) for Solid Tumours

In our invention, we explored a novel strategy to treat cancer by activate immunity against cancer cells. This was achieved by transfecting tumors with a set of proteins encoded by mRNA. This approach not only enhances the recognition of endogenous cancer cell antigens but also simultaneously reprograms the Tumor Microenvironment (TME). This strategy provides a broad-based immunotherapy strategy for various types of cancers.



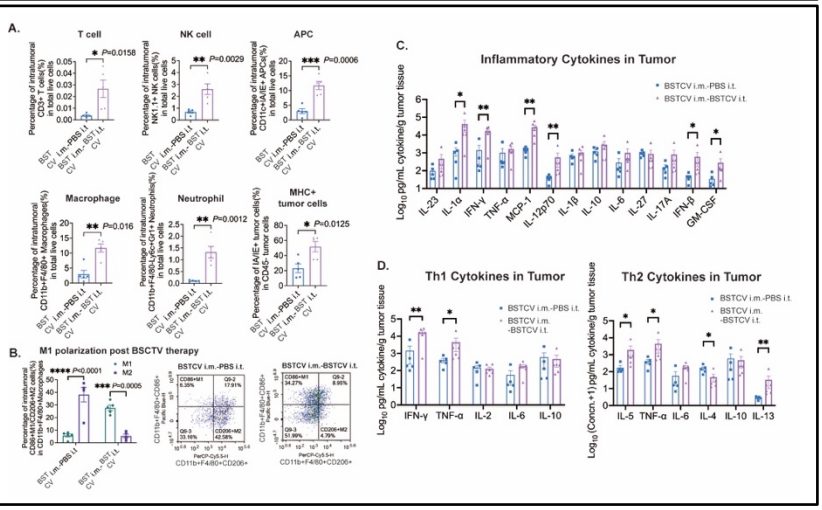
1. BSTCV has a potent cancer therapeutic efficacy in many different cancer types.

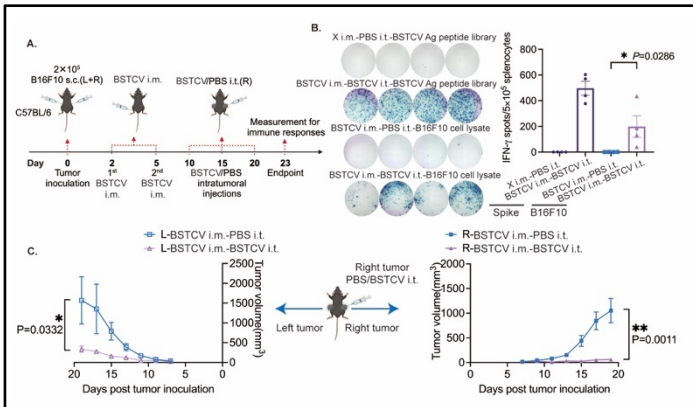
We observed profound inhibition of tumor growth (B16F10, CT26, MB49, and 4T1) in all treatment groups that received intratumoral injections of BSTCV compared to the control group that received intratumoral injections of PBS (A, C, D, E, F).

This was also supported by a marked improvement in the survival rate of mice bearing melanoma (B) and by a decrease in the 4T1 breast cancer lung metastasis (G).

2. Intratumoral BSTCV injection induces strong immune cell recruitment and TME reprogramming.

BSTCV therapy induces the recruitment of various immune cells into the tumor (T cells, NK cells, APCs, Macrophages, Neutrophils) (A), reversed the immunosuppressive TME to an anti-tumor phenotype (M2 to M1, increase the MHC expression in tumor) (A, B), and increased intratumoral or systemic Th1, Th2, and inflammatory-related cytokines (C, D), leading to positive therapeutic effects.





3. BSTCV treatment induces potent tumor antigen spreading and inhibits the growth of distal tumors.

Our study suggested intratumoral injection of BSTCV can induce potent antigen spreading to provoke broad tumor-specific anti-tumor T cell responses in hosts, not only the BSTCV encoding antigen-specific T cell responses (A, B). Additionally, the tumor growth inhibition was noted for nodules on both flanks of the mice not only the flank received BSTCV treatment, which suggested the BSTCV induced systemic anti-tumor responses (C). This result indicated the potential application of the BSTCV therapy in cancer patients with multiple tumor metastases.

4. Combination therapy of BSTCV and anti-PD-L1 effectively enhances therapeutic efficacy.

Interestingly, we observed a significant upregulation of CD274 (PD-L1) after intratumoral BSTCV injection by transcriptome analysis (A). Furthermore, our invention showed a combinational therapy potential with anti-PD-L1 therapy. Results suggested anti-PD-L1 therapy alone showed some inhibition of tumor growth but less than intratumoral BSTCV therapy alone when compared to the control group (B, C, D). Importantly, the combination therapy of BSTCV and anti-PD-L1 significantly enhanced the overall therapeutic efficacy compared to either BSTCV or anti-PD-L1 therapy alone (B, C, D). Our evidence clearly indicated anti-PD-L1 antibody treatment improved the overall therapeutic efficacy of BSTCV therapy in the melanoma model.