Recombinant CD80 fusion protein combined with Discoidin Domain Receptor 1 inhibitor for cancer treatment

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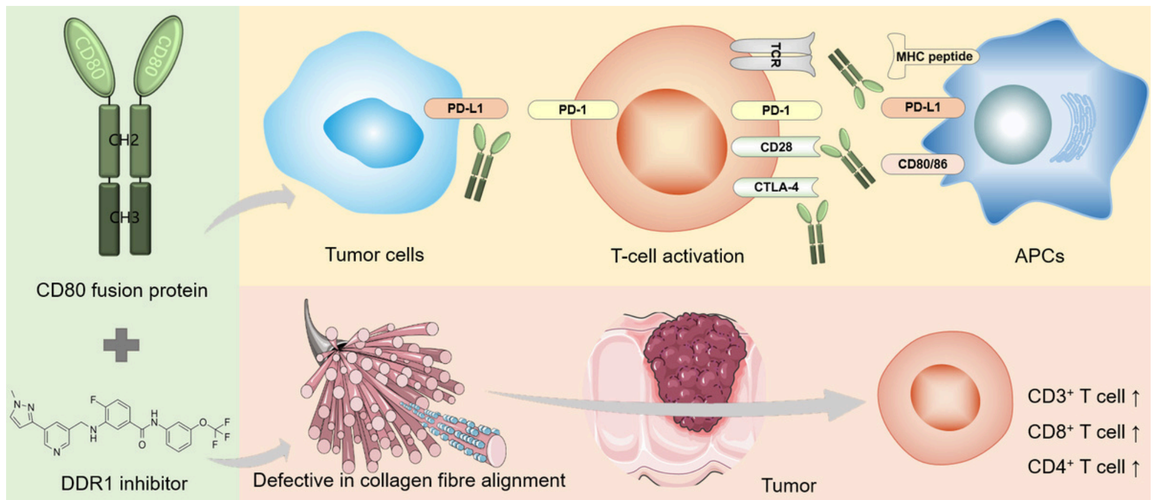
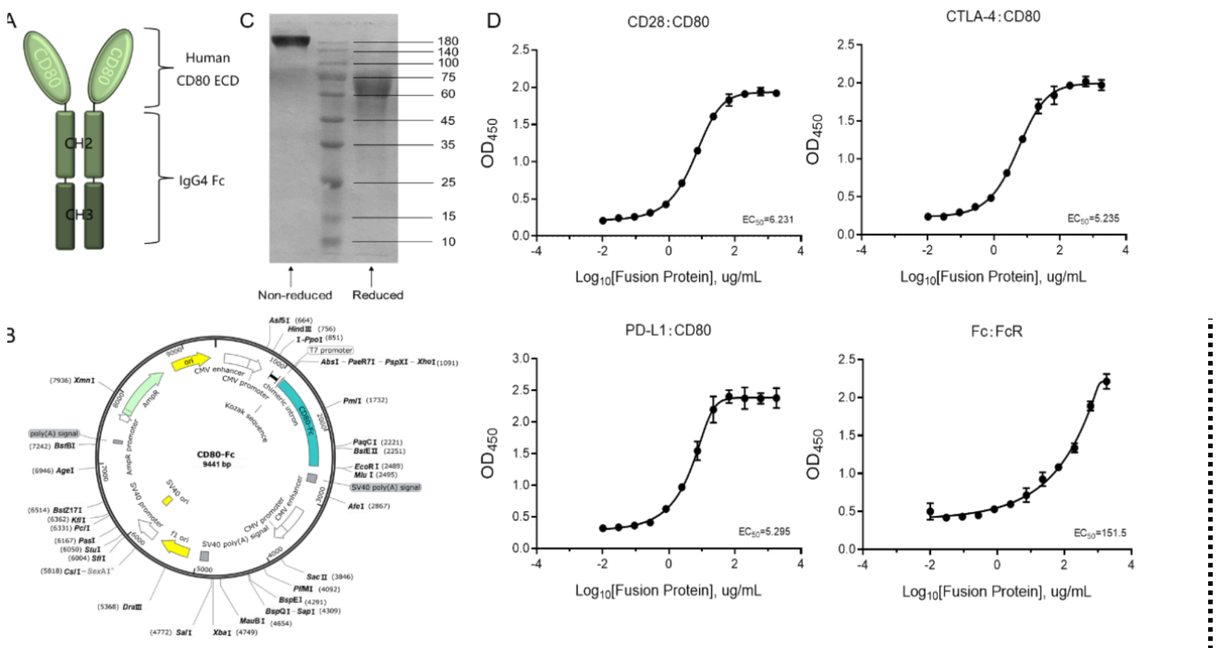
ABSTRACT

Immune checkpoint inhibitors (ICIs) have significantly advanced the field of cancer immunotherapy. However, clinical data has showed that many patients have a low response rate or even resistance to immune checkpoint inhibitor alone. The underlying reasons for its poor efficacy include the deficiency of immune infiltration and effective CD28/CD80 costimulatory signal in tumor. Discoidin domain receptor 1 (DDR1) has been reported to be negatively related to immune cell infiltration in the tumors. Herein, we constructed a soluble fusion protein using CD80, the natural ligand of CD28, in combination with DDR1 inhibitor. Our results demonstrated that CD80-Fc effectively activated T cells and inhibit tumor growth in vivo, even in tumors with poor efficacy of ICIs. Importantly, CD80-Fc fusion protein had a milder affinity against the targets which suggested a potential higher safety than CD28 agonists. Further, in order to promote tumor immune infiltration, we attempted to combine CD80-Fc fusion protein with DDR1 inhibitor for treatment. Our results indicated that using CD80-Fc fusion protein along with DDR1 inhibitor significantly promoted T cell infiltration in tumor microenvironment and more strongly inhibited tumor growth. Therefore, the combination use of CD80 fusion protein and DDR1 inhibitor could become an effective tumor immunotherapy strategy, potentially benefiting a larger number of patients.



RESULTS



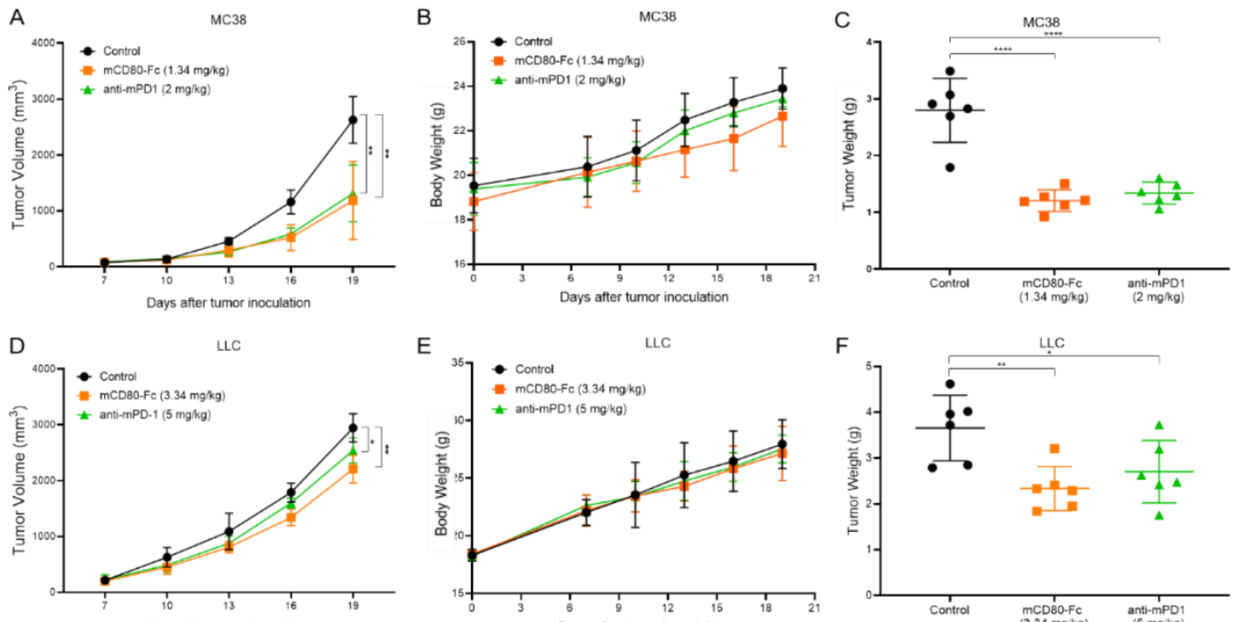
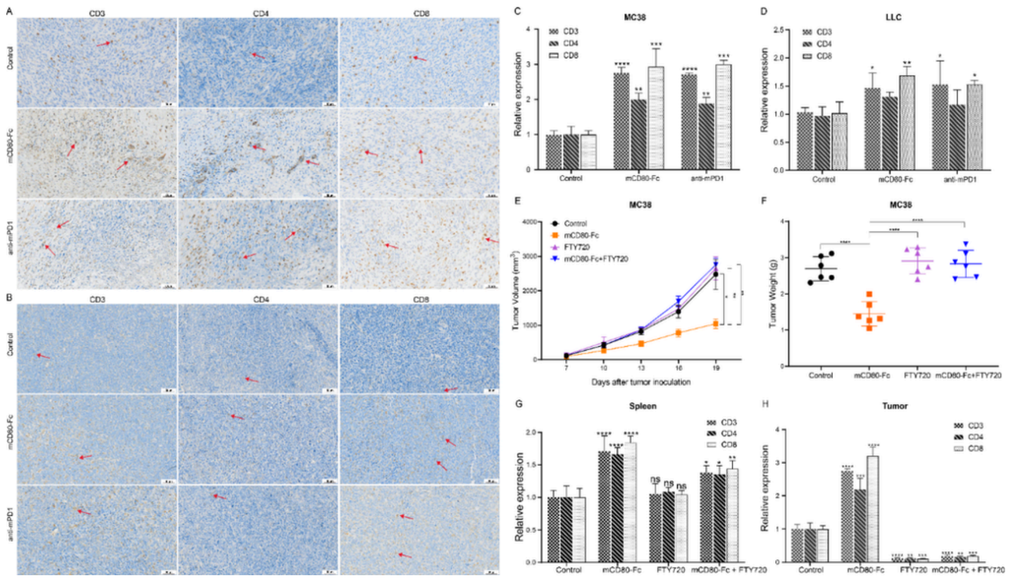


Fig. 1 Construction and expression of CD80-Fc fusion protein.

Fig. 2 CD80-Fc fusion protein has good anti-tumor activity in vivo.



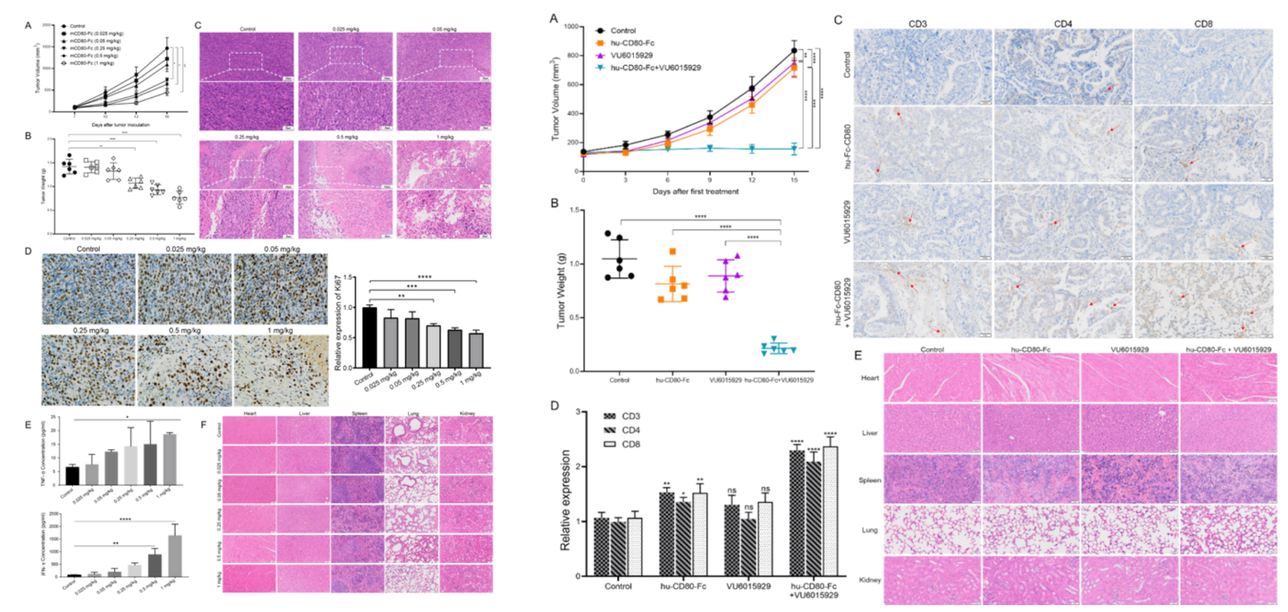


Fig. 3 The degree of immune infiltration affects the efficacy of CD80-Fc fusion protein.

Fig.4 CD80-Fc fusion protein has good safety and dose dependence. A Mice were administrated

Fig. 5 hu-CD80-Fc combined with DDR1 effectively inhibit tumor growth and promotinfiltration.

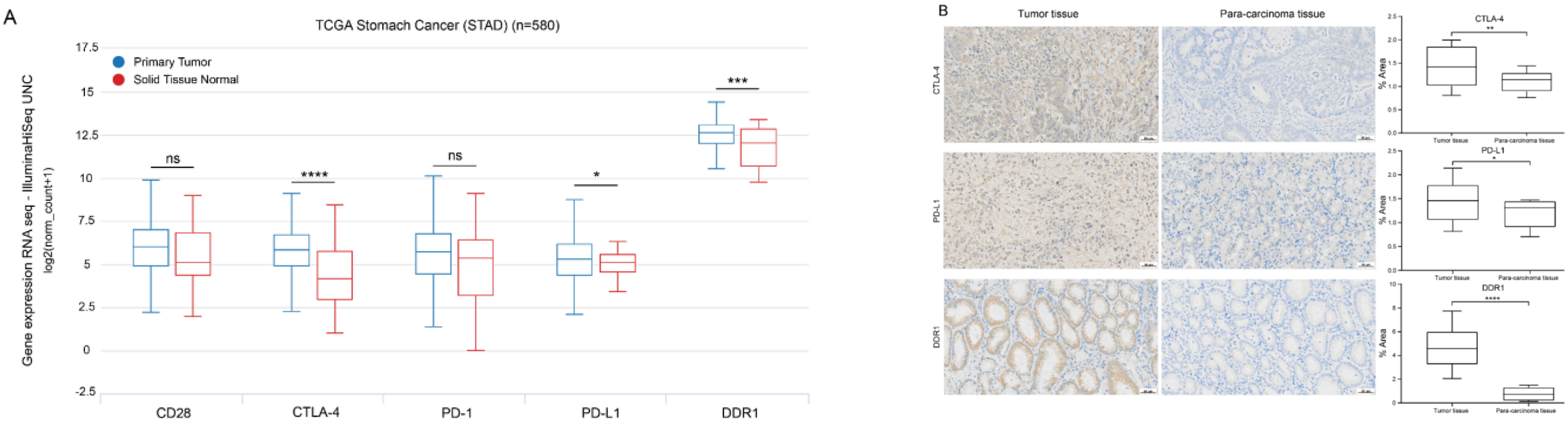


Fig.6 Significant overexpression of CTLA-4, PD-L1 and DDR1 in the gastric cancer.

CONCLUSIONS

1. The recombinant CD80 - Fc fusion protein was successfully constructed, expressed and purified, which can activate T cells, inhibit tumor growth, and has potential safety advantages.
2. The combination of CD80 - Fc fusion protein and DDR1 inhibitor significantly promotes T - cell infiltration in the tumor microenvironment and more potently suppresses tumor growth.
3. This combined treatment is expected to be an effective tumor immunotherapy strategy, potentially benefiting numerous cancer patients.

- Wang S, Hu P, Zhang X, Fan J, Zou J, Hong W, Huang X, Pan D, Chen H, Ju D, Zhu YZ, Ye L. Recombinant CD80 fusion protein combined with discoidin domain receptor 1 inhibitor for cancer treatment. Appl Microbiol Biotechnol. 2025 Feb 7;109(1):39. doi: 10.1007/s00253-025-13419-z.

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