Background Expression of radiation-induced immune escape molecules, including PD-L1, contributes to the efficacy of cancer immunotherapy.

Methods We used an unbiased in vivo gene knockdown screen in naïve T-cells and introduced them into irradiated host tumors to identify novel immunosuppressive genes activated during radiation.

Results From the screen, we found that butyrophilin 1A1 (BTN1A1) knockdown causes T-cell expansion in irradiated tumors. This points to the potential immune checkpoint role of BTN1A1. We validated that BTN1A1 expression is inducible in activated T-cells and that blocking BTN1A1 contributes to T-cell activation. Our data shown that knockout of BTN1A1 in CT26 colon tumor models shown dramatic defect of tumor growth, and the BTN1A1 ko CT26 tumors are more sensitive to radiotherapy. Moreover, we tested an anti-mouse BTN1A1 antibody (STC109) in mouse colon tumor models (CT26 tumors), we observed partial anti-tumor efficacy using single agent STC109, which was enhanced by the combination of STC109 with radiation. We also got similar result in in mouse lung tumor models (LLC tumors) using anti-mouse BTN1A1 antibody, and the combination treatment showed an improved suppression of tumor growth and lung metastasis compared to single agent.

Conclusions These findings indicate the role of BTN1A1 in tumor immune response from radiation stress, and that anti-BTN1A1 has strong potential to enhance efficacy of radiotherapy for cancer treatment.

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