新乡医学院
科技活动月 研究成果展

Attenuated *Salmonella* carrying IL-21 overexpression plasmid enhances radiotherapy efficacy in a preclinical model of melanoma

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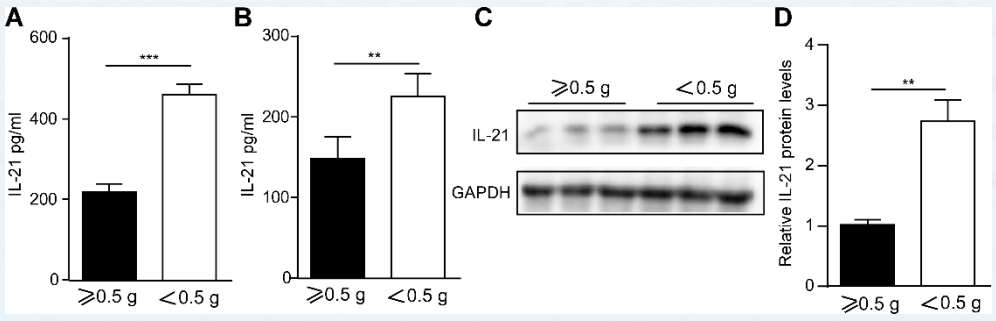
Introduction

Some melanoma patients exhibit substantial resistance to radiotherapy, with the underlying mechanisms of this resistance remaining elusive. Here, we found that Interleukin (IL)-21 expression was higher in the mice with good radiotherapy response to melanoma than in the mice with poor radiotherapy response. Interestingly, we also observed the higher infiltration of M2 TAMs and lower $CD8^+$ T cells in the group with poor radiotherapy response. To tackle this issue, we explored the therapeutic potential of a plasmid encoding IL-21, delivered via attenuated *Salmonella*, in mice bearing melanomas. Our findings revealed that IL-21 administration significantly reduced M2 TAMs infiltration and enhanced $CD8^+$ T cells infiltration and granzyme B (GZMB) expression within melanoma tumors. Most importantly, the combination of IL-21 with radiotherapy led to markedly tumor reduction compared to either treatment alone.

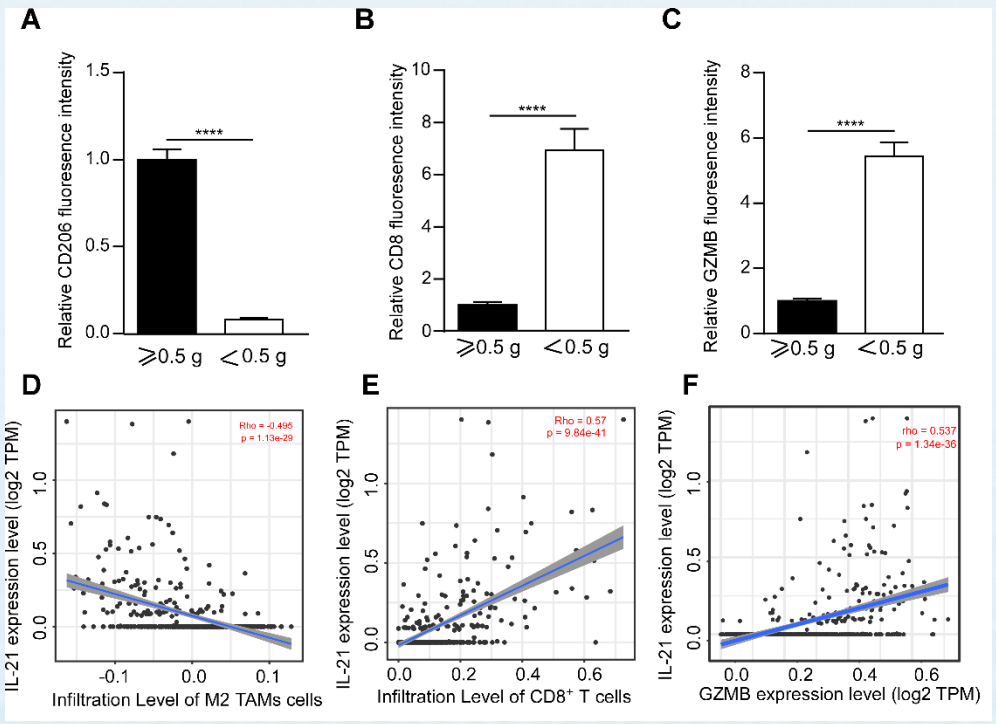
Methods

ELISA、Western blot、Immunofluorescence assay were performed to study the IL-21 was positively correlated with radiotherapy efficacy for mouse melanoma. Flow cytometry and Immunofluorescence assay were used to perform the effect of IL-21 on the infiltration of immune cells in the tumor microenvironment. The results of in vivo experiments show that attenuated *Salmonella* delivered IL-21 enhances radiotherapy's potent anti-tumor effects on mice with melanoma tumors.

Results

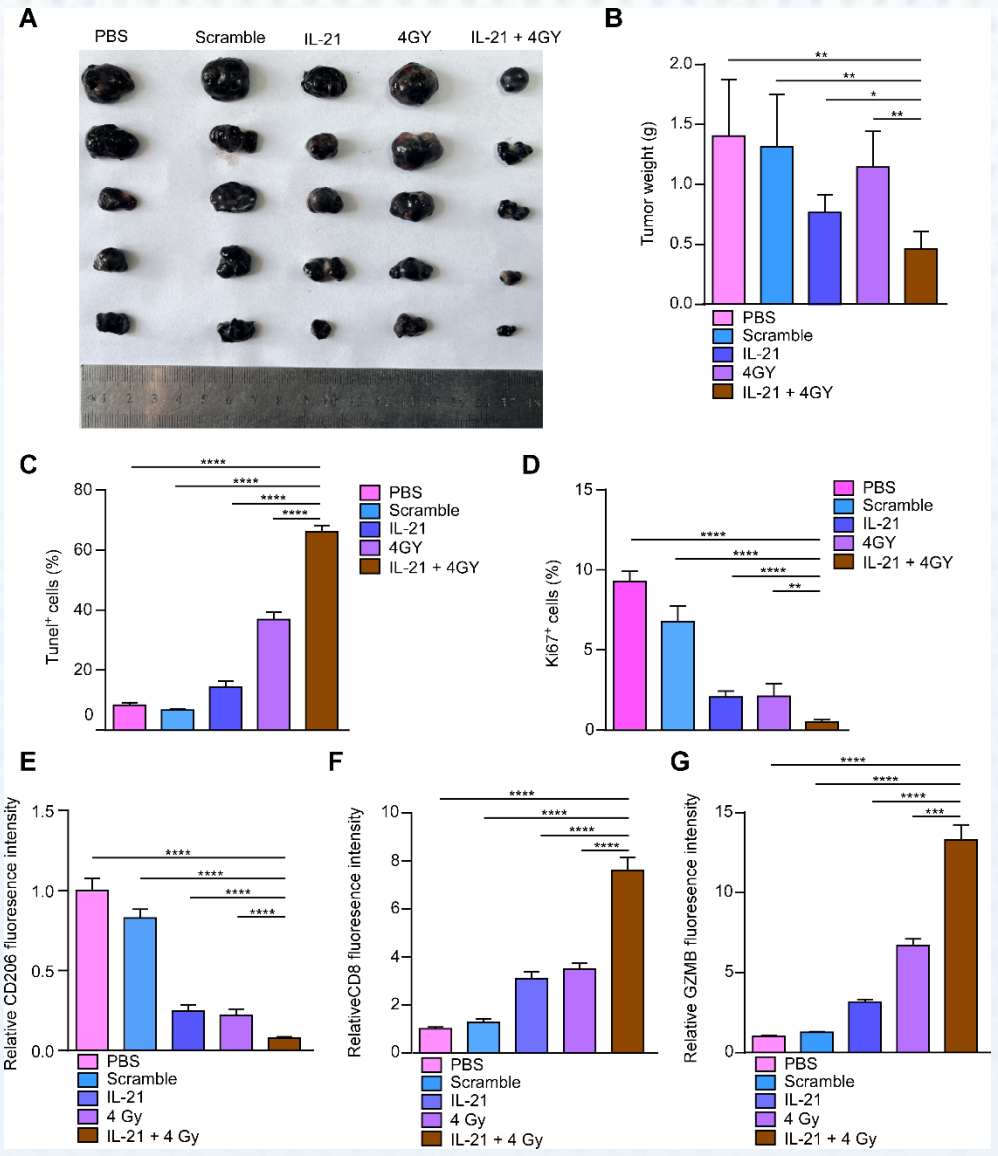


Our research identified a negative correlation between melanoma tumor weight and IL-21 expression levels in mice. We stratified subcutaneous melanoma mice into two groups based on their radiotherapy response: one with tumors ≥0.5 g and another with tumors <0.5 g.



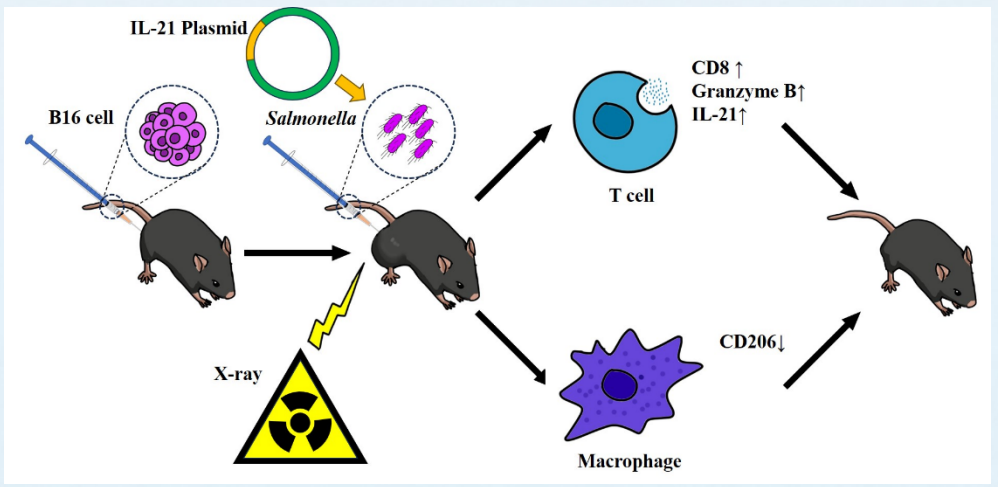
We also observed the higher infiltration of M2 TAMs and lower $CD8^+$T cells and GZMB in the group with poor radiotherapy response.

Results



our data shown that IL-21 administration notably boosted the radiotherapeutic efficacy against melanoma in mice. Meanwhile, IL-21 enhances radiotherapy-induced apoptosis in melanoma tumor cells and curbs their proliferation. Immunofluorescence results demonstrate that the IL-21 and radiotherapy combination not only decreased M2 TAM infiltration but also enhanced $CD8^+$ T cell infiltration and GZMB expression, suggesting that IL-21 can effectively bolster the antitumor immune response induced by radiotherapy.

Conclusion



Our findings reveal that combining IL-21 and radiotherapy markedly increased IL-21 expression within melanoma tumors. Furthermore, this combination approach significantly enhanced the infiltration of $CD8^+$ T cells and GZMB expression, while concurrently reducing the presence of M2 TAMs in melanoma tumors. These synergistic effects not only suppressed tumor growth but also strengthened antitumor immunity in B16 melanoma-bearing mice .