A novel cancer immunotherapy combines rMVA-CD40L with tumor targeting antibodies

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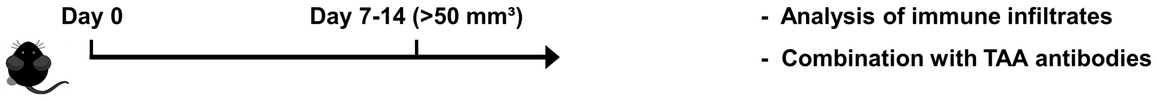
BACKGROUND

Virus-based vaccines and appropriate costimulation enhance potent antigen-specific T cell immunity against cancer.

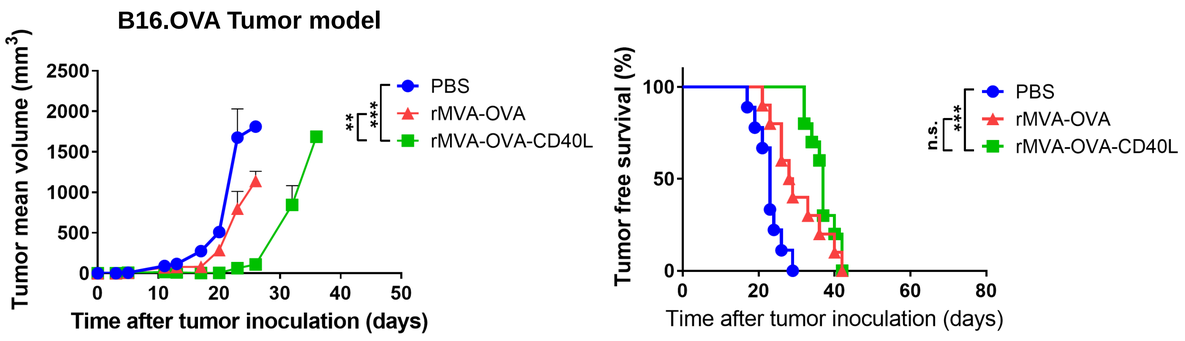
However, the tumor microenvironment exerts intrinsic and extrinsic mechanisms to evade tumor destruction.

Here we exploit both innate and adaptive immune responses triggered by a novel recombinant modified vaccinia virus Ankara (rMVA) encoding costimulatory CD40L against solid tumors in combination regimes to overcome tumor-induced resistance to immunotherapy.

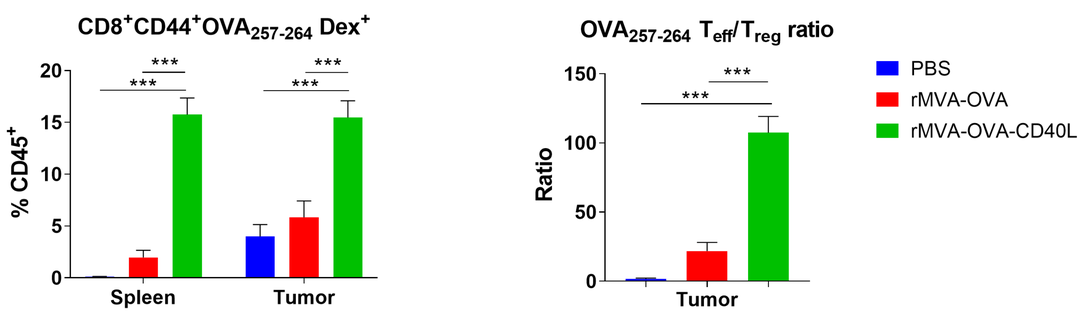
RESULTS



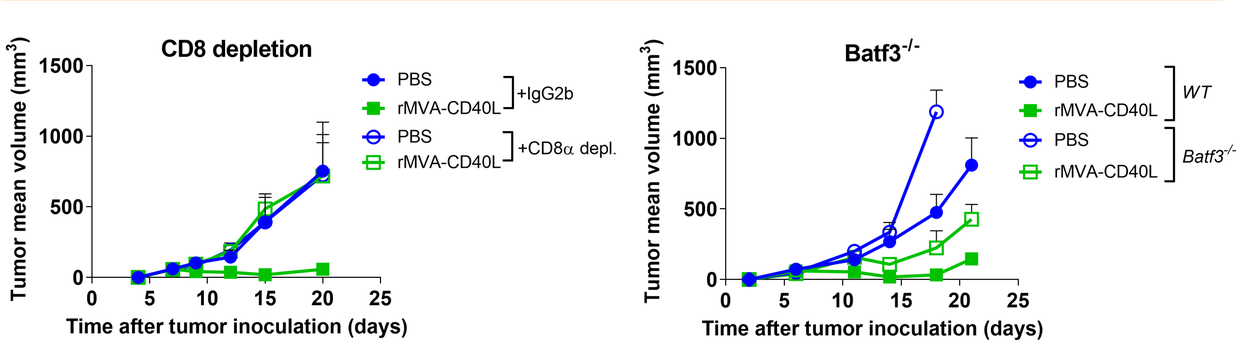
1) rMVA-CD40L PROMOTES TUMOR GROWTH CONTROL AND SURVIVAL IN UNRELATED TUMOR MODELS



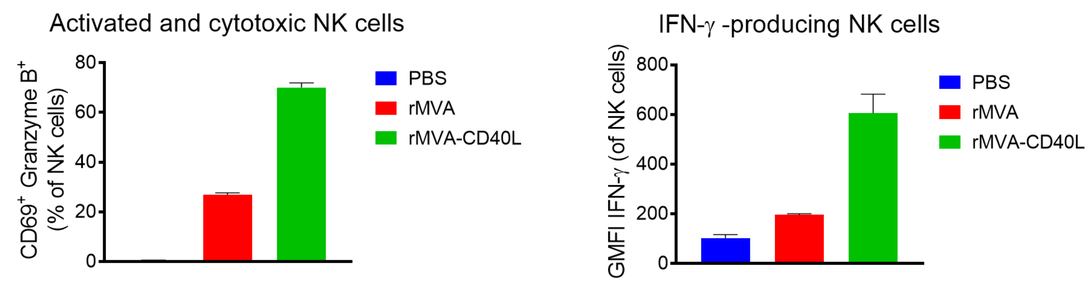
2) rMVA-CD40L INCREASES T CELL INFILTRATION OF ANTIGEN-SPECIFIC CD8⁺ T CELLS IN THE B16.OVA TUMOR MICROENVIRONMENT



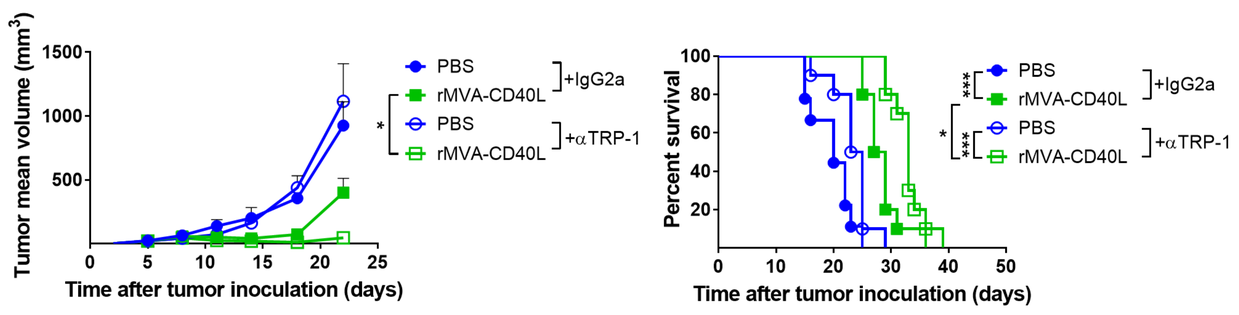
3) CD8⁺ T CELLS ARE ESSENTIAL FOR rMVA-CD40L INDUCED TUMOR GROWTH CONTROL; THERAPEUTIC EFFICACY IS ONLY PARTIALLY BATF3-DEPENDENT



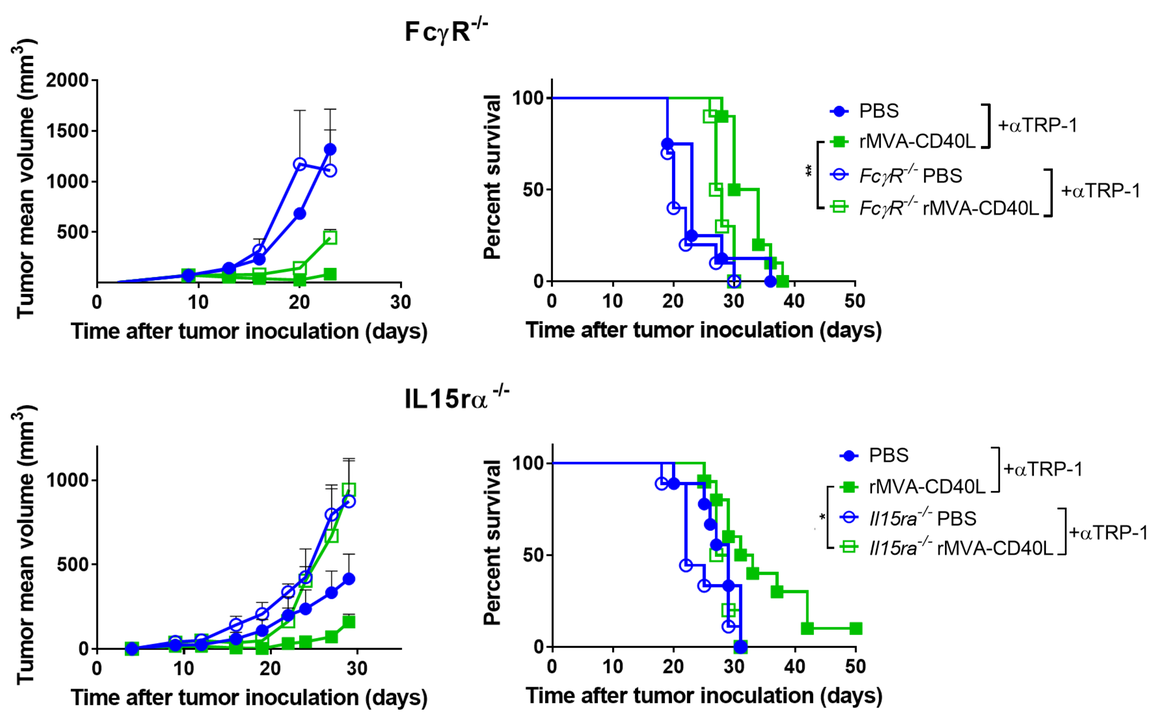
4) STRONG NK CELL ACTIVATION AND FUNCTION UPON SYSTEMIC rMVA-CD40L IMMUNIZATION



5) SYNERGISTIC EFFECT OF rMVA-CD40L WITH ANTI TRP-1 ANTIBODY *IN VIVO* IN THE B16.OVA TUMOR MODEL



6) SYNERGISTIC EFFECT OF rMVA-CD40L WITH ANTI TRP-1 ANTIBODY IS ABROGATED IN FcγR$^{-/-}$ AND IL15rα$^{-/-}$ MICE



CONCLUSION

- We describe a novel and translationally relevant therapeutic synergy between viral vaccination and CD40L costimulation.
- Taking advantage of intrinsic MVA-induced NK cell activation and function by CD40 ligation, we show strengthened antitumor immune responses when both rMVA-CD40L-induced innate and adaptive immune mechanisms are exploited by combining immunotherapeutic regimes.
- This finding has a potential positive impact in clinical trials where tumor targeting antibodies are currently under evaluation.

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