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

![Graph showing tumor growth control and survival](image1)

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

![Graph showing CD8+ T cell infiltration](image2)

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

![Graph showing CD8+ T cell depletion](image3)

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

![Graph showing NK cell activation](image4)

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

![Graph showing synergistic effect](image5)

6) SYNERGISTIC EFFECT OF rMVA-CD40L WITH ANTI TRP-1 ANTIBODY IS ABROGATED IN FcγR- AND IL15Rα- MICE

![Graph showing synergistic effect](image6)

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.