Oncolytic adenovirus type 3 coding for CD40L facilitates dendritic cell therapy of prostate cancer in humanized mice and patient samples

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Background

Dendritic cells (DCs) are vital antigen-presenting cells in the body. They play a crucial role in the detection and elimination of pathogens and cancer cells from the immune system. DCs based vaccination are safe and promising approach in cancer clinical trials. However, tumor immunosuppression in microenvironment destroys and weakens the function of DCs by hampering its maturation and activation. Hence, the outcomes of human clinical trial with DCs monotherapy is not always effective.

Methods

This study evaluates the therapeutic benefits of Ad3-hTERT-CMV-hCD40L virus and DCs in humanized mouse model. The cytotoxic ability of viruses is evaluated in vitro using prostate cancer histocultures obtained from patients.

Results

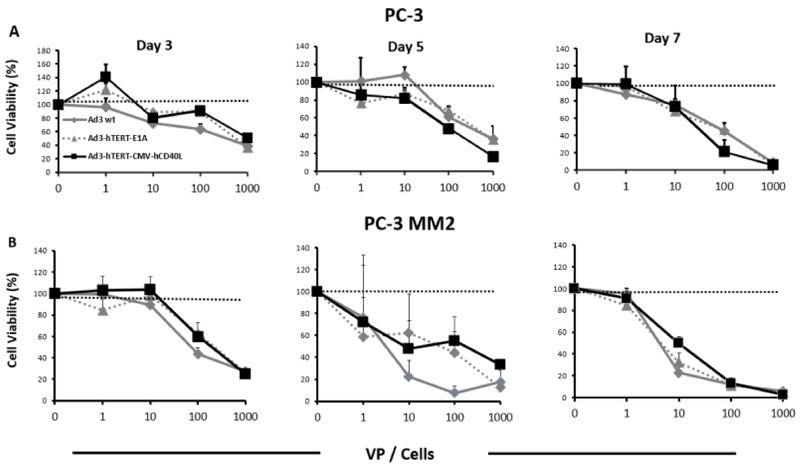


Figure 1. Oncolytic potency of Ad3-hTERT-CMVhCD40L assessed by MTS assay in PC-3 and PC3-MM2 cells at Day 3 and Day 5 and Day 7.

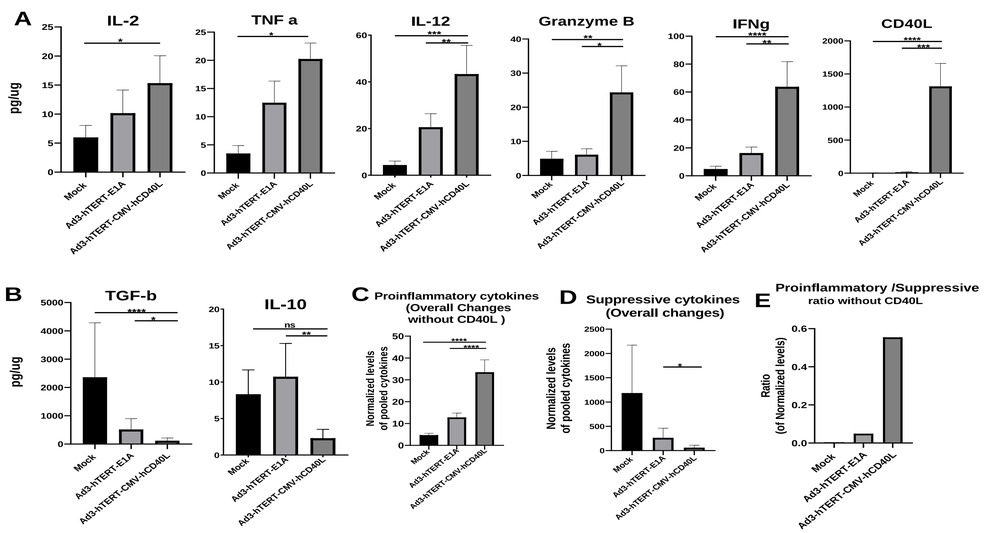


Figure 2. Overall changes in normalized pooled suppressive cytokines. The word ''overall changes'' indicates all analyzed proinflammatory or suppressive cytokine (such as IL2, TNFa, IL12, granzyme B, IFNg, TGF-b, IL10) except CD40L. The ratio of pro-inflammatory (without CD40L) vs suppressive normalized pooled cytokines.

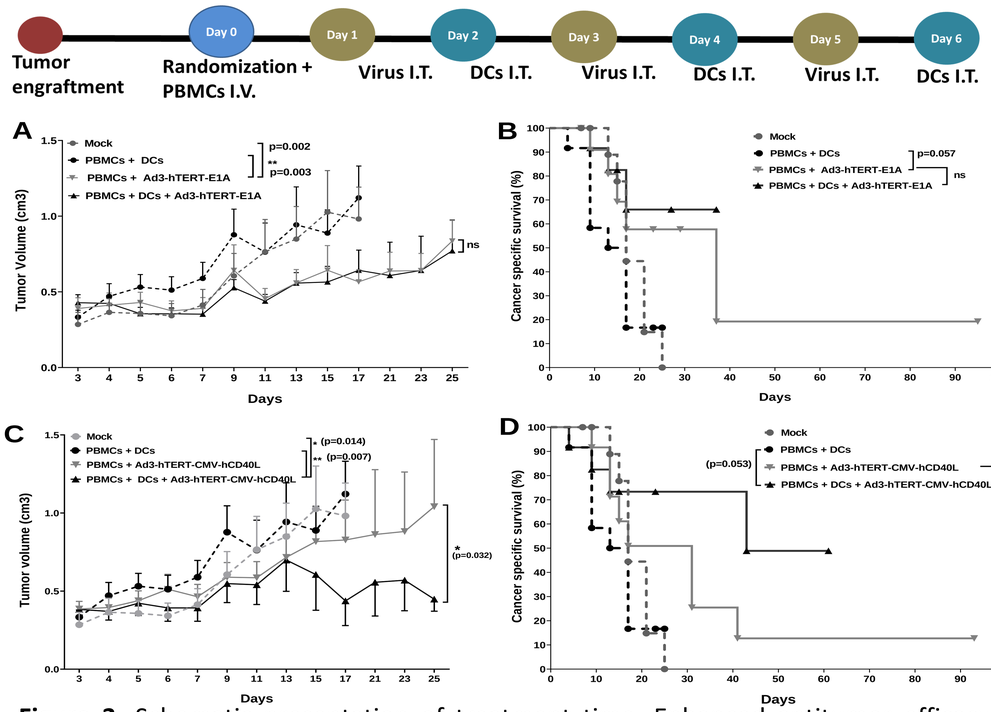
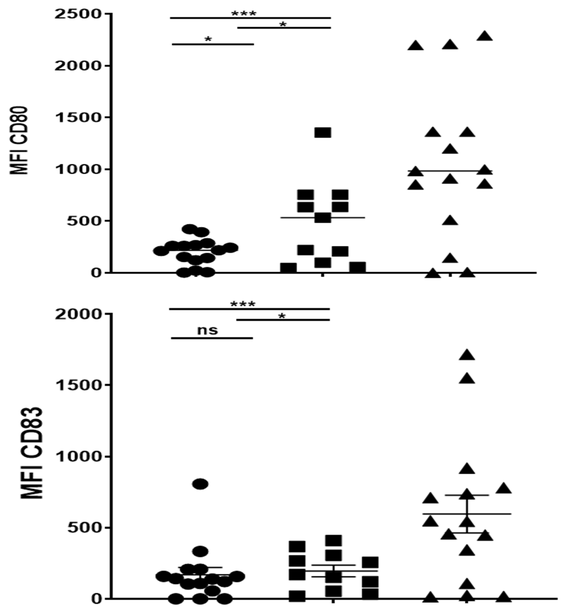


Figure 3. Schematic presentation of treatment time. Enhanced antitumor efficacy and cancer specific survival of humanized mice with subcutaneous PC3-MM2 tumors (A-D).



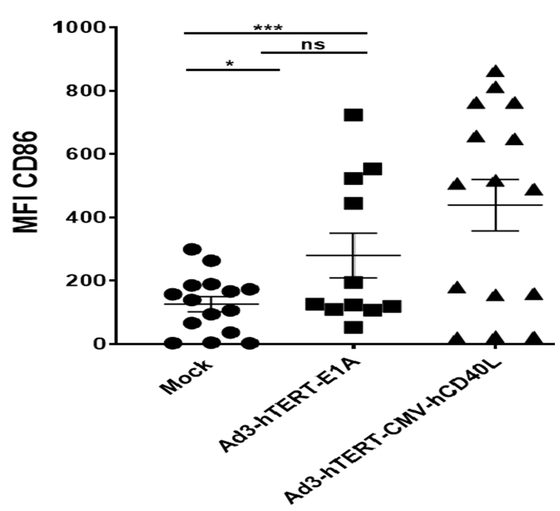


Figure 4. Virally expressed hCD40L induces DC maturation in patient samples.

Conclusions

Ad3-hTERT-CMV-hCD40L virus can modulate an immunosuppressive prostate tumor microenvironment. In particular, this virus could enable successful dendritic cell therapy in prostate cancer models and patient explants.