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TITLE:
Anti-cancer activity by photoimmunotherapy is driven by adaptive immune responses and vaccinates the host against the tumor

INTRODUCTION:
Photoimmunotherapy (PIT) is an investigational anti-cancer treatment platform utilizing cell-targeted antibodies conjugated to the IR700 (IRDye 700DX®) light-excitable dye. Upon illumination with non-thermal red light, target cells bound with antibody-conjugates undergo rapid necrosis. Previous work demonstrated that PIT induces features of immunogenic cell death of tumor cells and ignites an immune response against the tumor. In these preclinical studies, we investigated the extent to which the immune response contributes to the in vivo anti-cancer activity using syngeneic cancer models.

METHODS:
PIT treatment was applied to a panel of mouse and human cancer cell lines targeted by their respective antigen-binding conjugate in vitro, and the release of damage-associated molecular patterns (DAMPs) was measured from the cell supernatant. To determine the contribution of the immune response to PIT anti-cancer activity, PIT treatment was applied to immunocompetent animals with antibody-mediated CD8 T cell depletion, or blockade of CD40-CD40L axis concurrent with tumor implant or PIT treatment. To determine whether the immunogenic properties of PIT treatment induce vaccinal effects, immunocompetent animals were inoculated with in vitro PIT-treated cancer cells, and then challenged with live tumor cells in the contralateral flank one week later.

RESULTS:
Cancer cells treated with PIT released significant amounts of immunogenic cell death markers including DAMPs such as ATP and Annexin A1. The anti-cancer activity of PIT treatment in immunocompetent animals was inhibited when 1) pre-existing immunity was abrogated by blockade of the CD40-CD40L interaction at time of tumor implant, and 2) CD8 T cells were depleted from the animals. Applying CD40-CD40L blockade concurrent with PIT treatment partially abrogated anti-cancer activity. When animals were inoculated with cancer cells treated by PIT ex vivo, tumor rejection was achieved in 8 out of 9 animals when challenged with live tumor cells on the contralateral flank.
CONCLUSIONS:

Cancer treatment by PIT induces necrotic and immunogenic cell death resulting in local and systemic immune response. These preclinical data indicate that adaptive immune responses induced by PIT treatment drive the anti-cancer effects and can also provide vaccinal effects due to the release of DAMPs and cancer antigens.