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Enhancement of Abscopal Effect in Orthotopic Breast Cancer Animal Model With and Without Use of Nanoparticles as Radiosentizers

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INTRODUCTION

Currently radiation therapy (**RT**) primarily focuses on treatment of localized tumors, but a large majority of cancer deaths have been shown to be caused by secondary metastases. Over 90% of all cancer deaths occur due to the development of secondary metastases.[1] Nanoparticles, such a gold nanoparticles (**GNPs**), have been shown to act as radiosensitizers. The innovative technique in this investigation looks at the potential of boosting the **abscopal effect** using nanoparticles loaded with **Anti-CD40**.

- **GNPs** are added prior to **RT** to enhance the photoelectric effect, resulting in an increased damage to tumor cells and increase the RT therapeutic index[2]
- **Anti-CD40** would aid in the enhancement of the abscopal effect, anti-tumor tumor immune response, at distant metastatic sites as it recruits and and activates antigen presenting cells (APCs) within the tumor

Subcutaneous modulation was demonstrated using a subcutaneous and orthotopic tumor. Treatment was administered to the subcutaneous tumor, stemming from the observation that patients with breast cancer tend to express skin metastases at a significantly higher rate than other cancers.[3]

- In this investigation the treatment of the subcutaneous tumor will be used to represent the treatment of the metastatic skin cancer lesion, where the orthotopic tumor will be used to represent the untreated primary tumor in the breast.
- Due to the abundance of APCs in the skin, the treatment of the subcutaneous may provide a more efficient route for the use of the abscopal effect.

AIM

The study's purpose was to investigate the potential in enhancing the abscopal effect, an anti-tumor response to distant metastatic sites, with gold nanoparticles (**GNPs**) in combination with radiation therapy (**RT**) and **anti-CD40** as an immunoadjuvant.

METHOD

Cell Culture:

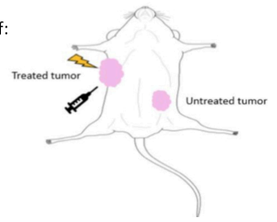
- The cell lined used was PY230, it was cultured in DMEM media

Tumor Inoculation:

- Female C57/BL6 mice were injected with PY230, one subcutaneously (left) and one orthotopically (right)

Treatment:

- Once tumors developed, mice were randomized
- The subcutaneous tumor was the treated tumor, it was treated with combinations of:
  - 6Gy RT per subcutaneous tumor using the SARRP (Small Animal Radiation Research Platform)
  - GNPs (0.5 mg/tumor)
  - Anti-CD40 as an immunoadjuvant (20ug/tumor)
- Tumor sizes were measured to assess treatment



CONCLUSIONS

- The data shows that the abscopal effect is most observed when using the combination treatment of RT+AntiCD40+GNP
- The combination treatment used the GNPs to enhance the photoelectric effect intratumorally, therefore more damage of the cancer cells and increased release of neoantigens. Anti-CD40 recruits and activates APCs within the tumor. AntiCD40 then aided in the enhancement of the anti-tumor immune response at distant metastatic sites.
- These results warrant further studies for an in-depth determination of the significance of GNPs functionalized with AntiCD40 in the enhancement of the abscopal effect. These results justify further investigations towards developing the subcutaneous modulated abscopal effect, which could extend RT treatment for metastatic breast cancer

RESULTS

In-vivo Results:

- The abscopal effect was exhibited in the non-treated, orthotopic tumor in the combination treatment of RT+AntiCD40+GNP
- Overall less tumor growth in the treated, subcutaneous tumor that was treated with the combination treatment of RT+AntiCD40+GNP
- On day 35, in the treated group, the control had 4.2 times higher tumor growth and the RT group had 2.8 times higher tumor growth than the combination treatment of RT+AntiC40+GNP
- On day 35, in the non-treated group, the control had 1.9 times higher tumor growth and the RT group had 2.4 times tumor growth than the combination treatment of RT+AntiCD40+GNP

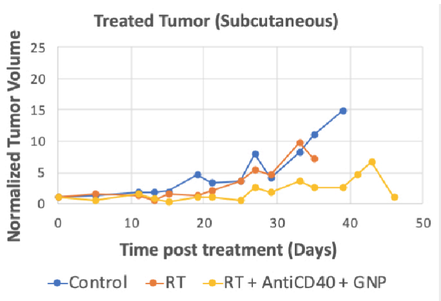


Figure 2: Normalized treated tumor (subcutaneous) measurements for all three treatment cohorts

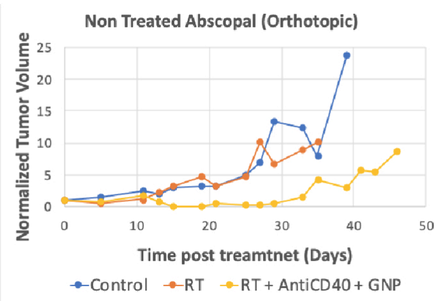


Figure 3: Normalized non treated tumor (orthotopic) measurements for all three treatment cohorts

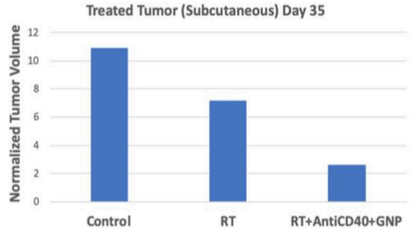


Figure 4: Normalized treated tumor (subcutaneous) measurements for day 35 after treatment

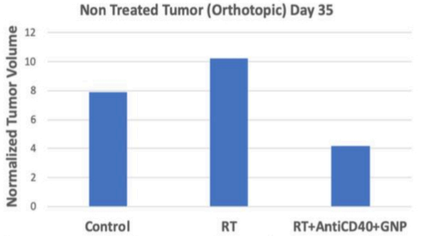


Figure 5: Normalized non treated tumor (subcutaneous) measurements for day 35 after treatment

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